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IDS Flag Clearance for Application 10678816

IDS Information

Content	Mailroom Date	Entry Number	IDS Review	Reviewer
M844	02-23-2004	18	☑	06-27-2006 09:13:08 LBristol
M844	02-14-2005	21	☑	06-27-2006 09:13:08 LBristol

UPDATE

Limits: **Publication Date to 2002/10/4**

- Search History will be lost after eight hours of inactivity.
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- Search numbers may not be continuous; all searches are represented.
- Click on query # to add to strategy

Search	Most Recent Queries	Time	Result
#5	Search **hepsin antibody** Limits: **Publication Date to 2002/10/4**	12:36:56	2
#3	Search **(hepsin) and antibody** Limits: **Publication Date to 2002/10/4**	12:35:14	2
#2	Search **(modified hepsin) and antibody** Limits: **Publication Date to 2002/10/4**	12:28:09	0
#1	Search **(hepsin variant) and antibody** Limits: **Publication Date to 2002/10/4**	12:27:52	0

Clear History

Jun 21 2006 12:14:26

WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Tuesday, June 27, 2006

Hide?	Set Name	Query	Hit Count
	DB=PGPB; PLUR=YES; OP=ADJ		
☐	L18	(10678816)	0
☐	L17	(10678816)[APN]	0
	DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ		
☐	L16	(10678816)	0
☐	L15	(L14 and liposome)	30
☐	L14	(L13 and (therapeutic agent))	31
☐	L13	(L12 and (cytotoxic adj agent))	31
☐	L12	(L11 and hybridoma)	50
☐	L11	(L10 and fragment)	57
☐	L10	(L9 and neutraliz$)	57
☐	L9	(L8 and humaniz$)	123
☐	L8	(L6 and (chimer$ or immunoconjugate))	194
☐	L7	L6 and chimer$ or immunoconjugate	5693
☐	L6	(hepsin) and (immunoglobulin or antibody)	274
☐	L5	(modified adj hepsin) and (immunoglobulin or antibody)	4
☐	L4	L3	3
	DB=PGPB,USPT; PLUR=YES; OP=ADJ		
☐	L3	L1 and (modified adj hepsin)	3
	DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ		
☐	L2	L1 and (hepsin variant)	3
☐	L1	hepsin and antibody	272

END OF SEARCH HISTORY

Welcome to DialogClassic Web(tm)

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 Dialog level 05.12.03D
Last logoff:  26jun06 11:13:49
Logon file001 27jun06 14:21:32
          *** ANNOUNCEMENTS ***
                    ***
NEW FILES RELEASED
***Trademarkscan - South Korea (File 655)
***Regulatory Affairs Journals (File 183)
***Index Chemicus (File 302)
***Inspec (File 202)

RESUMED UPDATING
***File 141, Reader's Guide Abstracts
                    ***
RELOADS COMPLETED
***File 516, D&B--Dun's Market Identifiers
***File 523, D&B European Dun's Market Identifiers
***File 531, American Business Directory
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*** The 2005 reload of the CLAIMS files (Files 340, 341, 942)
is now available online.
                                  ***
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***File 468, Public Opinion Online (POLL)
Chemical Structure Searching now available in Prous Science Drug
Data Report (F452), Prous Science Drugs of the Future (F453),
IMS R&D Focus (F445/955), Pharmaprojects (F128/928), Beilstein
Facts (F390), Derwent Chemistry Resource (F355) and Index Chemicus
(File 302).
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File   1:ERIC 1966-2006/May
       (c) format only 2006 Dialog

      Set  Items  Description
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Cost is in DialUnits
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B 155, 159, 10, 203, 35, 5, 467, 73, 434, 34
       27jun06 14:22:03 User290558 Session D56.1
            $0.81    0.232 DialUnits File1
     $0.81  Estimated cost File1
     $0.13  INTERNET
     $0.94  Estimated cost this search
     $0.94  Estimated total session cost   0.232 DialUnits

SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R) 1950-2006/Jun 26
         (c) format only 2006 Dialog
  File 159:Cancerlit 1975-2002/Oct
         (c) format only 2002 Dialog
 *File 159: Cancerlit is no longer updating.
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Please see HELP NEWS159.
  File  10:AGRICOLA 70-2006/May
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        (c) 2006 The Thomson Corporation
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        (c) 2001 Informania Ltd.
 *File 467: F467 will close on February 1, 2006.                    7.
  File  73:EMBASE 1974-2006/Jun 27
        (c) 2006 Elsevier Science B.V.
  File 434:SciSearch(R) Cited Ref Sci 1974-1989/Dec
        (c) 1998 Inst for Sci Info
  File  34:SciSearch(R) Cited Ref Sci 1990-2006/Jun W4
        (c) 2006 Inst for Sci Info

      Set  Items  Description
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?

S (HEPSIN  (W) PROTEIN) OR (HEPSIN (W) PEPTIDE) OR (HEPSIN (W) FRAGMENT)
            356  HEPSIN
        6773173  PROTEIN
              6  HEPSIN(W)PROTEIN
            356  HEPSIN
        1145042  PEPTIDE
              0  HEPSIN(W)PEPTIDE
            356  HEPSIN
         524135  FRAGMENT
              0  HEPSIN(W)FRAGMENT
      S1      6  (HEPSIN  (W) PROTEIN) OR (HEPSIN (W) PEPTIDE) OR (HEPSIN
                 (W) FRAGMENT)
?

RD S1
      S2      4  RD S1  (unique items)
?


Set     Items   Description
S1          6   (HEPSIN  (W) PROTEIN) OR (HEPSIN (W) PEPTIDE) OR (HEPSIN (-
             W) FRAGMENT)
S2          4   RD S1  (unique items)
?

S (HEPSIN  (W) PROTEIN)  AND (ANTIBODY OR IMMUNOGLOBULIN)
            356  HEPSIN
        6773173  PROTEIN
              6  HEPSIN(W)PROTEIN
        1758086  ANTIBODY
         732972  IMMUNOGLOBULIN
      S3      1  (HEPSIN  (W) PROTEIN)  AND (ANTIBODY OR IMMUNOGLOBULIN)
?


Set     Items   Description
S1          6   (HEPSIN  (W) PROTEIN) OR (HEPSIN (W) PEPTIDE) OR (HEPSIN (-
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             W) FRAGMENT)
S2           4   RD S1  (unique items)
S3           1   (HEPSIN  (W) PROTEIN)  AND (ANTIBODY OR IMMUNOGLOBULIN)
?

S (HEPSIN (W) PEPTIDE) AND (ANTIBODY OR IMMUNOGLOBULIN)
              356  HEPSIN
          1145042  PEPTIDE
                0  HEPSIN(W)PEPTIDE
          1758086  ANTIBODY
           732972  IMMUNOGLOBULIN
      S4        0  (HEPSIN (W) PEPTIDE) AND (ANTIBODY OR IMMUNOGLOBULIN)
?


Set     Items   Description
S1          6   (HEPSIN  (W) PROTEIN) OR (HEPSIN (W) PEPTIDE) OR (HEPSIN (-
             W) FRAGMENT)
S2          4   RD S1  (unique items)
S3          1   (HEPSIN  (W) PROTEIN)  AND (ANTIBODY OR IMMUNOGLOBULIN)
S4          0   (HEPSIN (W) PEPTIDE) AND (ANTIBODY OR IMMUNOGLOBULIN)
?

S (HEPSIN (W) FRAGMENT) AND (ANTIBODY OR IMMUNOGLOBULIN)
              356  HEPSIN
           524135  FRAGMENT
                0  HEPSIN(W)FRAGMENT
          1758086  ANTIBODY
           732972  IMMUNOGLOBULIN
      S5        0  (HEPSIN (W) FRAGMENT) AND (ANTIBODY OR IMMUNOGLOBULIN)
?


Set     Items   Description
S1          6   (HEPSIN  (W) PROTEIN) OR (HEPSIN (W) PEPTIDE) OR (HEPSIN (-
             W) FRAGMENT)
S2          4   RD S1  (unique items)
S3          1   (HEPSIN  (W) PROTEIN)  AND (ANTIBODY OR IMMUNOGLOBULIN)
S4          0   (HEPSIN (W) PEPTIDE) AND (ANTIBODY OR IMMUNOGLOBULIN)
S5          0   (HEPSIN (W) FRAGMENT) AND (ANTIBODY OR IMMUNOGLOBULIN)
?

TYPE S3/MEDIUM,K/1

  3/K/1     (Item 1 from file: 73)
DIALOG(R)File  73:EMBASE
(c) 2006 Elsevier Science B.V. All rts. reserv.

11336092     EMBASE No: 2001350575
 Integrating DNA and tissue microarrays cancer profiling
  Ibarrola N.; Pandey A.
  AUTHOR EMAIL: nibarrola@bmb.sdu.dk
  Trends in Biochemical Sciences ( TRENDS BIOCHEM. SCI. ) (United Kingdom)
  01 OCT 2001, 26/10 (589)
  CODEN: TBSCD   ISSN: 0968-0004
  DOCUMENT TYPE: Journal ; Note
  LANGUAGE: ENGLISH
  NUMBER OF REFERENCES: 1

DRUG DESCRIPTORS:
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...DNA; prostate specific antigen--endogenous compound--ec; serine
proteinase; protein; protein serine threonine kinase; protein  antibody ;
proteome; biological marker; unclassified drug
DRUG TERMS (UNCONTROLLED): protein  hepsin ;  protein  pim 1
?


Set     Items   Description
S1          6   (HEPSIN  (W) PROTEIN) OR (HEPSIN (W) PEPTIDE) OR (HEPSIN (-
             W) FRAGMENT)
S2          4   RD S1  (unique items)
S3          1   (HEPSIN  (W) PROTEIN)  AND (ANTIBODY OR IMMUNOGLOBULIN)
S4          0   (HEPSIN (W) PEPTIDE) AND (ANTIBODY OR IMMUNOGLOBULIN)
S5          0   (HEPSIN (W) FRAGMENT) AND (ANTIBODY OR IMMUNOGLOBULIN)
?

S (HEPSIN AND (ANTIBODY OR IMMUNOGLOBULIN))
           356  HEPSIN
       1758086  ANTIBODY
        732972  IMMUNOGLOBULIN
      S6    16  (HEPSIN AND (ANTIBODY OR IMMUNOGLOBULIN))
?

RD S6
      S7    11  RD S6  (unique items)
?

TYPE S7/FULL/1-11

  7/9/1     (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
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20762310   PMID: 16585186
 Antibodies neutralizing hepsin protease activity do not impact cell
 growth but inhibit invasion of prostate and ovarian tumor cells in culture.
  Xuan Jian-Ai; Schneider Doug; Toy Pam; Lin Rick; Newton Alicia; Zhu Ying;
Finster  Silke; Vogel David; Mintzer Bob; Dinter Harald; Light David; Parry
Renate; Polokoff Mark; Whitlow Marc; Wu Qingyu; Parry Gordon
  Department  of  Cancer  Research, Berlex Biosciences, 2600 Hilltop Drive,
Richmond, CA 94806, USA.
  Cancer  research (United  States)  Apr  1 2006,  66  (7)  p3611-9,  ISSN
0008-5472--Print  Journal Code: 2984705R
  Publishing Model Print
  Document type: Journal Article
  Languages: ENGLISH
  Main Citation Owner: NLM
  Record type: MEDLINE; Completed
  Subfile:   INDEX MEDICUS
  Hepsin  is  a  type II transmembrane serine protease that is expressed in
normal  liver, and at lower levels in kidney, pancreas, and testis. Several
studies  have  shown  that  hepsin  mRNA  is significantly elevated in most
prostate  tumors,  as  well  as a significant fraction of ovarian and renal
cell carcinomas and hepatomas. Although the overexpression of mRNA in these
tumors  has  been  extensively  documented,  there  has  been  conflicting
literature  on  whether  hepsin  plays  a  role  in  tumor  cell growth and
progression. Early literature implied a role for hepsin in human tumor cell
proliferation,  whereas  recent  studies  with a transgenic mouse model for
prostate  cancer  support  a  role  for  hepsin  in  tumor  progression and
metastases.  To  evaluate  this  issue  further,  we  have  expressed an
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activatable form of hepsin, and have generated a set of monoclonal antibodies that neutralize enzyme activity. The neutralizing antibodies inhibit hepsin enzymatic activity in biochemical and cell-based assays. Selected neutralizing and nonneutralizing antibodies were used in cell-based assays with tumor cells to evaluate the effect of antibodies on tumor cell growth and invasion. Neutralizing antibodies failed to inhibit the growth of prostate, ovarian, and hepatoma cell lines in culture. However, potent inhibitory effects of the antibodies were seen on invasion of ovarian and prostate cells in transwell-based invasion assays. These results support a role for hepsin in tumor cell progression but not in primary tumor growth. Consistent with this, immunohistochemical experiments with a mouse monoclonal antibody reveal progressively increased staining of prostate tumors with advanced disease, and in particular, extensive staining of bone metastatic lesions.

Tags: Female; Male

Descriptors: *Antibodies, Monoclonal--pharmacology--PD; *Ovarian Neoplasms--enzymology--EN; *Prostatic Neoplasms--enzymology--EN; *Serine Endopeptidases--metabolism--ME; *Serine Proteinase Inhibitors--pharmacology --PD; Amino Acid Sequence; Antibodies, Monoclonal--immunology--IM; Cell Growth Processes--drug effects--DE; Cell Growth Processes--physiology--PH; Cell Line, Tumor; Cloning, Molecular; Humans; Immunohistochemistry; Molecular Sequence Data; Neoplasm Invasiveness; Ovarian Neoplasms--drug therapy--DT; Ovarian Neoplasms--pathology--PA; Prostatic Neoplasms--drug therapy--DT; Prostatic Neoplasms--pathology--PA; Recombinant Proteins --biosynthesis--BI; Recombinant Proteins--genetics--GE; Serine Endopeptidases--biosynthesis--BI; Serine Endopeptidases--genetics--GE; Serine Endopeptidases--immunology--IM; Serine Proteinase Inhibitors --immunology--IM

CAS Registry No.: 0 (Antibodies, Monoclonal); 0 (Recombinant Proteins) ; 0 (Serine Proteinase Inhibitors)

Enzyme No.: EC 3.4.21 (Serine Endopeptidases); EC 3.4.21.- (hepsin)

Record Date Created: 20060404

Record Date Completed: 20060522

7/9/2 (Item 2 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

15284824 PMID: 15627507

Identification and characterization of hepsin/-TM, a non-transmembrane hepsin isoform.

Li Yang; Yu Zhenbao; Zhao Xin; Shen Shi-Hsiang

Mammalian Cell Genetics, Biotechnology Research Institute, National Research Council of Canada, Montreal, Quebec, Canada H4P 2R2.

Biochimica et biophysica acta (Netherlands) Jan 11 2005, 1681 (2-3) p157-65, ISSN 0006-3002--Print Journal Code: 0217513

Publishing Model Print-Electronic

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Type II transmembrane serine proteases (TTSPs), including hepsin, are a new class of cell surface catalytic enzymes. In the present study, a non-transmembrane isoform of hepsin, named hepsin/-TM that originates from alternative splicing, was identified. Unlike the transmembrane hepsin isoform, this non-transmembrane isoform was distributed within the cytoplasm. Real-time PCR experiments revealed that while hepsin was expressed in all tested human tissues, hepsin/-TM was restricted in kidney,

brain and lung tissues. Significantly, hepsin/-TM was not expressed in liver where hepsin was originally identified. However, hepsin/-TM was highly expressed in brain where hepsin was expressed at a relatively lower level. Moreover, these two isoforms showed different expression patterns in a number of colon adenocarcinoma cell lines. In addition, in contrast to hepsin, expression of hepsin/-TM in vivo does not exert any apparent inhibitory effect on mammalian cell growth.

Descriptors: *Colonic Neoplasms--metabolism--ME; *Serine Endopeptidases --genetics--GE; Epithelial Cells--metabolism--ME; Fluorescent Antibody Technique; Humans; Kidney--metabolism--ME; Organ Specificity--physiology --PH; Protein Isoforms--genetics--GE; Protein Isoforms--metabolism--ME; Protein Structure, Tertiary; Sequence Analysis, Protein; Serine Endopeptidases--metabolism--ME; Tumor Cells, Cultured

CAS Registry No.: 0 (Protein Isoforms)

Enzyme No.: EC 3.4.21 (Serine Endopeptidases); EC 3.4.21.- (hepsin)

Record Date Created: 20050103

Record Date Completed: 20050309

Date of Electronic Publication: 20041215

7/9/3 (Item 3 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

14407372 PMID: 12744720

Mouse matriptase-2: identification, characterization and comparative mRNA expression analysis with mouse hepsin in adult and embryonic tissues.

Hooper John D; Campagnolo Luisa; Goodarzi Goodarz; Truong Tony N; Stuhlmann Heidi; Quigley James P

Division of Vascular Biology, Department of Cell Biology, The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA.

Biochemical journal (England) Aug 1 2003, 373 (Pt 3) p689-702, ISSN 0264-6021--Print Journal Code: 2984726R

Contract/Grant No.: CA55852; CA; NCI; HL31950; HL; NHLBI; HL65738; HL; NHLBI; T32 HL07695; HL; NHLBI

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

We report the identification and characterization of mouse matriptase-2 (m-matriptase-2), an 811-amino-acid protein composed of an N-terminal cytoplasmic domain, a membrane-spanning domain, two CUB (complement protein subcomponents C1r/C1s, urchin embryonic growth factor and bone morphogenetic protein 1) domains, three LDLR (low-density-lipoprotein receptor class A) domains and a C-terminal serine-protease domain. All m-matriptase-2 protein domain boundaries corresponded with intron/exon junctions of the encoding gene, which spans approx. 29 kb and comprises 18 exons. Matriptase-2 is highly conserved in human, mouse and rat, with the rat matriptase-2 gene (r-maltriptase-2) predicted to encode transmembrane and soluble isoforms. Western-blot analysis indicated that m-matriptase-2 migrates close to its theoretical molecular mass of 91 kDa, and immunofluorescence analysis was consistent with the proposed surface membrane localization of this protein. Reverse-transcription PCR and in-situ -hybridization analysis indicated that m-matriptase-2 expression overlaps with the distribution of mouse hepsin (m-hepsin, a cell-surface serine protease identified in hepatoma cells) in adult tissues and during embryonic development. In adult tissues both are expressed at highest levels in liver, kidney and uterus. During embryogenesis m-matriptase-2

expression peaked between days 12.5 and 15.5. m-hepsin expression was biphasic, with peaks at day 7.5 to 8.5 and again between days 12.5 and 15.5. In situ hybridization of embryonic tissues indicated abundant expression of both m-matriptase-2 and m-hepsin in the developing liver and at lower levels in developing pharyngo-tympanic tubes. While m-hepsin was detected in the residual embryonic yolk sac and with lower intensity in lung, heart, gastrointestinal tract, developing kidney tubules and epithelium of the oral cavity, m-matriptase-2 was absent in these tissues, but strongly expressed within the nasal cavity by olfactory epithelial cells. Mechanistic insight into the potential role of this new transmembrane serine protease is provided by its novel expression profile in embryonic and adult mouse.

Descriptors: *Embryo--metabolism--ME; *Membrane Proteins--metabolism--ME; *RNA, Messenger--genetics--GE; *Serine Endopeptidases--genetics--GE; *Serine Endopeptidases--metabolism--ME; Amino Acid Sequence; Animals; Base Sequence; CHO Cells; Comparative Study; Cricetinae; DNA; Fluorescent Antibody Technique; Hela Cells; Humans; In Situ Hybridization; Membrane Proteins--chemistry--CH; Membrane Proteins--genetics--GE; Mice; Molecular Sequence Data; Rats; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.; Sequence Homology, Amino Acid; Serine Endopeptidases --chemistry--CH

Molecular Sequence Databank No.: GENBANK/AY055383; GENBANK/AY055384; GENBANK/AY234104; GENBANK/AY240929; GENBANK/BK000520

CAS Registry No.: 0 (Membrane Proteins); 0 (RNA, Messenger); 9007-49-2 (DNA)

Enzyme No.: EC 3.4.21 (Serine Endopeptidases); EC 3.4.21.- (hepsin); EC 3.4.21.- (matriptase); EC 3.4.21.- (matriptase 2)

Record Date Created: 20030722

Record Date Completed: 20030903

7/9/4 (Item 4 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

10368677 PMID: 7814421

Hepsin, a putative membrane-associated serine protease, activates human factor VII and initiates a pathway of blood coagulation on the cell surface leading to thrombin formation.

Kazama Y; Hamamoto T; Foster D C; Kisiel W

Department of Pathology, University of New Mexico School of Medicine, Albuquerque 87131.

Journal of biological chemistry (UNITED STATES) Jan 6 1995, 270 (1) p66-72, ISSN 0021-9258--Print Journal Code: 2985121R

Contract/Grant No.: HL35246; HL; NHLBI

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Previous studies have shown that hepsin is a putative membrane-associated serine protease that is required for cell growth (Torres-Rosado, A., O'Shea, K. S., Tsuji, A., Chou, S.-H., and Kurachi, K. (1993) Proc. Natl. Acad. Sci. U.S. A. 90, 7181 7185). In the present study, we have transfected baby hamster kidney (BHK) cells with a plasmid containing the cDNA for human hepsin and examined these cells for their ability to activate several blood coagulation factors including factors X, IX, VII, prothrombin, and protein C. Little, if any, proteolytic activation of factors X, IX, prothrombin, or protein C was observed when these clotting

factors were incubated with hepsin-transfected cells. On the other hand, hepsin-transfected cells proteolytically activated significant concentrations of human factor VII in a time- and calcium-dependent manner, whereas essentially no activation of factor VII was observed in BHK cells transfected with plasmid lacking the cDNA for hepsin. The factor VII activating activity in the hepsin-transfected BHK cell line was confined exclusively to the total membrane fraction and was inhibited > 95% by antibody raised against a fusion protein consisting of maltose-binding protein and the extracellular domain of human hepsin. An active site factor VII mutant, S344A factor VII, was cleaved as readily as plasma-derived factor VII by hepsin-transfected cells, indicating that factor VII was not converted to factor VIIa autocatalytically on the cell surface. In contrast, an activation cleavage site factor VII mutant, R152E factor VII, was not cleaved by hepsin-transfected cells, suggesting that factor VII and S344A factor VII were activated on these cells by cleavage of the Arg152-Ile153 peptide bond. In the copresence of factor VII and factor X, hepsin-transfected BHK cells supported the formation of factor Xa. In addition, in the copresence of factor VII, factor X, and prothrombin, hepsin-transfected BHK cells supported the formation of thrombin. These results strongly suggest that membrane-associated hepsin converts zymogen factor VII to factor VIIa, which in turn, is capable of initiating a coagulation pathway on the cell surface that ultimately leads to thrombin formation.

Descriptors: *Blood Coagulation; *Factor VII--metabolism--ME; *Membrane Proteins--metabolism--ME; *Serine Endopeptidases--metabolism--ME; *Thrombin --biosynthesis--BI; Animals; Base Sequence; Cell Membrane--metabolism--ME; Cells, Cultured; Cricetinae; Factor X--metabolism--ME; Humans; Molecular Sequence Data; Prothrombin--metabolism--ME; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.; Trypsin--metabolism--ME

CAS Registry No.: 0 (Membrane Proteins); 9001-25-6 (Factor VII); 9001-26-7 (Prothrombin); 9001-29-0 (Factor X)

Enzyme No.: EC 3.4.21 (Serine Endopeptidases); EC 3.4.21.- (hepsin); EC 3.4.21.4 (Trypsin); EC 3.4.21.5 (Thrombin)

Record Date Created: 19950203

Record Date Completed: 19950203

7/9/5 (Item 5 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

08933803 PMID: 1885621

Hepsin, a cell membrane-associated protease. Characterization, tissue distribution, and gene localization.

Tsuji A; Torres-Rosado A; Arai T; Le Beau M M; Lemons R S; Chou S H; Kurachi K

Department of Human Genetics, University of Michigan Medical School, Ann Arbor 48109.

Journal of biological chemistry (UNITED STATES) Sep 5 1991, 266 (25) p16948-53, ISSN 0021-9258--Print Journal Code: 2985121R

Contract/Grant No.: HL38644; HL; NHLBI

Publishing Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Subfile: INDEX MEDICUS

Hepsin, a putative membrane-bound serine protease, was originally identified as a human liver cDNA clone (Leytus, S.P., Loeb, K.R., Hagen, F.S., Kurachi, K., and Davie, E.W. (1988) Biochemistry 27, 1067-1074). In

the present study the human hepsin gene was localized to chromosome 19 at q11-13.2. The messenger RNA of hepsin is 1.85 kilobases in size and present in most tissues, with the highest level in liver. Hepsin is synthesized as a single polypeptide chain, and its mature form of 51 kDa was found in various mammalian cells including HepG2 cells and baby hamster kidney cells. It is present in the plasma-membrane in a molecular orientation of type II membrane-associated proteins, with its catalytic subunit (carboxyl-terminal half) at the cell surface, and its amino terminus facing the cytosol. Hepsin is found neither in cytosol nor in culture media. The results obtained suggest that hepsin has an important role(s) in cell growth and function.

Descriptors: *Chromosomes, Human, Pair 19; *Serine Endopeptidases --genetics--GE; Amino Acid Sequence; Animals; Cell Line; Cell Membrane --enzymology--EN; Chromosome Mapping; Fluorescent Antibody Technique; Gene Expression; Humans; Immunoblotting; Molecular Sequence Data; Molecular Weight; Organ Specificity--genetics--GE; Research Support, Non-U.S. Gov't; Research Support, U.S. Gov't, P.H.S.; Serine Endopeptidases--metabolism--ME

Enzyme No.: EC 3.4.21 (Serine Endopeptidases); EC 3.4.21.- (hepsin)

Record Date Created: 19911004

Record Date Completed: 19911004

7/9/6 (Item 1 from file: 35)

DIALOG(R)File 35:Dissertation Abs Online

02045450 ORDER NO: AADAA-I0807170

Identification and characterization of human oviductal cell derived embryotrophic factor 3

Author: Lee, Yin Lau

Degree: Ph.D.

Year: 2004

Corporate Source/Institution: University of Hong Kong (People's Republic of China) (0842)

Source: VOLUME 65/10-B OF DISSERTATION ABSTRACTS INTERNATIONAL. PAGE 4994.

Descriptors: BIOLOGY, MOLECULAR

Descriptor Codes: 0307

The objectives of this study are to investigate the effect of a human oviduct derived embryotrophic factor, embryotrophic factor-3 (ETF-3) on the gene expression of mouse preimplantation embryo and to determine the identity of ETF-3. Human oviductal epithelial cells (OE) were immortalized (OE-E6/E7) and characterized. OE-E6/E7 retains a number of characteristics of OE. It possessed human oviductal specific glycoprotein, estrogen receptors, cytokeratin and strong telomerase activities. The development of preimplantation mouse embryo was significantly better after cocultured with OE-E6/E7 and cultured in medium supplemented with OE-E6/E7 derived ETF-3 when compared to medium alone culture. This cell line was used for subsequent studies.

The mRNA expression patterns of the ETF-3 treated embryos were studied at the blastocyst stage by mRNA differential display (DDRT-PCR). Twelve of the differentially expressed genes that had high homology with cDNA sequences in the GenBank were selected for further characterization. The differential expressions of ezrin, heat shock 70kD protein 5, cytochrome c oxidase subunit VIIa-L precursor, proteinase activated receptor 2, eukaryotic translation initiation factor 2β, cullin 1 and proliferating cell nuclear antigen were confirmed by RT-PCR. The results demonstrated that OE-E6/E7 produced ETF-3 that influenced gene expression of mouse blastocyst.

It is hypothesized that the higher hatching and blastulation rate after ETF-3 treatment may be due to the alteration of gene expression related to these processes related genes. Hepsin and Na/K-ATPase expression had been implicated in these processes respectively. TaqMan real-time quantitative PCR (qPCR) was used to quantify the mRNA copy number of these two genes in mouse embryos with or without ETF-3 treatment. The expression of hepsin in mouse blastocysts was very low but detectable and unaffected by ETF-3 treatment. ETF-3 treated and in vivo developed embryos had significantly higher Na/K-ATPase-β1 subunit expression than medium alone culture indicated that ETF-3 produced by OE-E6/E7 increased the Na/K-ATPase-β1 expression of the treated embryos. Monoclonal anti-ETF-3 antibody that abolished the embryotrophic activity of ETF-3 recognized a 115-kDa protein in the ETF-3 preparation. The protein was identified by mass spectrometry analysis to be complement C3.

Immuno-cross-reactivities between ETF-3 and C3 proteins using anti-C3 and anti-ETF-3 antibodies confirmed the identities of ETF-3. Derivatives of C3, C3b and iC3b but not C3, were embryotrophic. iC3b was most efficient in enhancing the development of blastocysts with larger size and higher hatching rate, consistent with the previous reported embryotrophic activity of ETF-3. Embryos treated with iC3b contained iC3b immunoreactivity. The oviductal epithelium produced C3 as C3 immunoreactivity and mRNA were detected in epithelium of human fallopian tube and OE-E6/E7. Cyclical changes of C3 expression were also found in the mouse oviduct with the highest expression at the estrus stage. Molecules involving in the conversion of Cab to iC3b and for binding of iC3b were present in the human oviduct (factor 1) and mouse preimplantation embryo (Crry, CR3), respectively. The present data showed that the oviduct produced C3/C3b, which was converted to iC3b to stimulate embryo development. The mechanism of iC3b on preimplantation embryo development remained to be investigated.

7/9/7 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

12508758 EMBASE No: 2004090618
Immunological treatment of ovarian cancer
Cannon M.J.; Santin A.D.; O'Brien T.J.
M.J. Cannon, Dept. of Microbiology and Immunology, Univ. of AR for Medical Sciences, 4301 West Markham, Little Rock, AR 72205 United States

AUTHOR EMAIL: mcannon@uams.edu
Current Opinion in Obstetrics and Gynecology (CURR. OPIN. OBSTET. GYNECOL.) (United Kingdom) 2004, 16/1 (87-92)
CODEN: COOGE ISSN: 1040-872X
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 32

Purpose of review: Development of immunological treatments for ovarian cancer has not been a conspicuous success story over the past few years. Only a handful of clinical trials have reported immunological responses, and correlation with clinical benefit has been elusive. Several recent studies presented in this review, however, point to a revival of optimism for the development of novel immunotherapeutic strategies. Recent findings: The cloning and sequencing of CA125, coupled with novel structural and functional insights, undoubtedly represent important steps forward. The possibility that CA125 could play a role in evasion of immunity by ovarian tumors may represent a new challenge, but does not detract from its potential as a therapeutic target. Of the recent clinical trial reports,

the most intriguing results were seen from immunotherapy with a conventional mouse monoclonal antibody specific for CA125, in which human anti-mouse antibody responses correlated significantly with improved survival of patients with advanced stage ovarian cancer and clinical evidence of recurrent disease at the time of treatment. Summary: There is little doubt that CA125 will undergo a renaissance as an important target antigen for development of novel immunological treatments, particularly with regard to cellular therapies. Identification of other novel ovarian tumor antigens will also accelerate research focused on stimulation of T-cell immunity. Current research trends suggest a paradigm shift in emphasis from vaccines designed to elicit antibody responses to strategies such as dendritic cell vaccination that are designed to induce broader immunity, including ovarian tumor antigen-specific helper T-lymphocyte and cytotoxic T-lymphocyte responses.

BRAND NAME/MANUFACTURER NAME: theratope/Biomira/Canada; herceptin
MANUFACTURER NAMES: Biomira/Canada
DRUG DESCRIPTORS:
CA 125 antigen--endogenous compound--ec; carbohydrate antigen--clinical trial--ct; carbohydrate antigen--drug therapy--dt; carbohydrate antigen --pharmacology--pd; cancer vaccine--clinical trial--ct; cancer vaccine --drug therapy--dt; cancer vaccine--pharmacology--pd; mucin 1--clinical trial--ct; mucin 1--drug therapy--dt; mucin 1--pharmacology--pd; antineoplastic agent--drug therapy--dt; antineoplastic agent--pharmacology --pd; monoclonal antibody--adverse drug reaction--ae; monoclonal antibody --clinical trial--ct; monoclonal antibody--drug therapy--dt; monoclonal antibody--pharmacology--pd; idiotypic antibody--clinical trial--ct; idiotypic antibody--drug therapy--dt; idiotypic antibody--pharmacology--pd; epidermal growth factor receptor 2--clinical trial--ct; epidermal growth factor receptor 2--drug combination--cb; epidermal growth factor receptor 2 --drug therapy--dt; epidermal growth factor receptor 2--pharmacology--pd; epidermal growth factor receptor 2--intradermal drug administration--dl; granulocyte macrophage colony stimulating factor--clinical trial--ct; granulocyte macrophage colony stimulating factor--drug combination--cb; granulocyte macrophage colony stimulating factor--drug therapy--dt; granulocyte macrophage colony stimulating factor--pharmacology--pd; granulocyte macrophage colony stimulating factor--intradermal drug administration--dl; peptide--clinical trial--ct; peptide--drug combination --cb; peptide--drug therapy--dt; peptide--pharmacology--pd; peptide --intradermal drug administration--dl; tumor antigen--clinical trial--ct; tumor antigen--drug combination--cb; tumor antigen--drug therapy--dt; tumor antigen--endogenous compound--ec; tumor antigen--pharmacology--pd; tumor antigen--intradermal drug administration--dl; trastuzumab--drug therapy--dt ; trastuzumab--pharmacology--pd; serine proteinase--endogenous compound--ec ; kallikrein--endogenous compound--ec; neuropsin--endogenous compound--ec; paclitaxel--pharmacology--pd; doxorubicin--pharmacology--pd; gemcitabine --pharmacology--pd; protein p53--endogenous compound--ec; unclassified drug
MEDICAL DESCRIPTORS:
*ovary cancer--drug therapy--dt; *cancer immunotherapy
molecular cloning; amino acid sequence; protein function; antigen structure ; drug targeting; cancer survival; treatment outcome; drug efficacy; correlation analysis; antibody response; cancer staging; cancer recurrence; vaccination; cancer chemotherapy; autologous hematopoietic stem cell transplantation; drug toxicity--side effect--si; cytotoxic T lymphocyte; cellular immunity; gene overexpression; breast cancer--drug therapy--dt; lung non small cell cancer--drug therapy--dt; dendritic cell; adoptive immunotherapy; cancer control; cancer resistance; immunomodulation; human; clinical trial; review; priority journal
DRUG TERMS (UNCONTROLLED): sialyl Tn keyhole limpet hemocyanin conjugate vaccine--clinical trial--ct; sialyl Tn keyhole limpet hemocyanin conjugate

vaccine--drug therapy--dt; sialyl Tn keyhole limpet hemocyanin conjugate vaccine--pharmacology--pd; murine monoclonal antibody B43.13--drug therapy --dt; murine monoclonal antibody B43.13--pharmacology--pd; murine monoclonal idiotypic antibody ACA125--clinical trial--ct; murine monoclonal idiotypic antibody ACA125--drug therapy--dt; murine monoclonal idiotypic antibody ACA125--pharmacology--pd; monoclonal antibody c MOV18--adverse drug reaction--ae; monoclonal antibody c MOV18--drug therapy--dt; monoclonal antibody c MOV18--pharmacology--pd; hepsin--endogenous compound --ec; stratum corneum chymotryptic enzyme--endogenous compound--ec; tumor associated differentially expressed gene product 12--endogenous compound --ec; tumor associated differentially expressed gene product 14--endogenous compound--ec; testisin--endogenous compound--ec; tumor associated differentially expressed gene product 15--endogenous compound--ec; tumor associated differentially expressed gene product 16--endogenous compound --ec; theratope
CAS REGISTRY NO.: 212255-06-6 (mucin 1); 137632-09-8 (epidermal growth factor receptor 2); 180288-69-1 (trastuzumab); 37259-58-8 (serine proteinase); 8006-48-2, 9001-01-8 (kallikrein); 171715-15-4 (neuropsin) ; 33069-62-4 (paclitaxel); 23214-92-8, 25316-40-9 (doxorubicin); 103882-84-4 (gemcitabine)
SECTION HEADINGS:
010 Obstetrics and Gynecology
016 Cancer
037 Drug Literature Index
038 Adverse Reaction Titles

7/9/8 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

11940475 EMBASE No: 2003046875
Identifying immunotherapeutic targets for prostate carcinoma through the analysis of gene expression profiles
Nelson P.S.
P.S. Nelson, Divisions of Hum. Biol./Clin. Res., Fred Hutchinson Cancer Res. Center, 1100 Fairview Ave. North, 04-100, Seattle, WA 98109-1024 United States
AUTHOR EMAIL: pnelson@fhcrc.org
Annals of the New York Academy of Sciences (ANN. NEW YORK ACAD. SCI.) (United States) 2002, 975/- (232-245)
CODEN: ANYAA ISSN: 0077-8923
DOCUMENT TYPE: Journal ; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 80

Carcinoma of the prostate represents one of the most frequently diagnosed cancers in men. If detected at an early stage, prostate cancer is highly treatable. However, cancers identified at a late stage are rarely cured with contemporary medical therapies. Early detection strategies presently center on the identification of prostate-specific proteins in the serum, and emerging therapeutics have utilized genes and proteins with prostate-restricted expression for tissue-selective immunological regimens incorporating vaccines, dendritic cell therapy, gene therapy, and antibody-based cell targeting. In order to develop improved therapeutic procedures, efforts have been directed toward the identification of genes exhibiting prostate-restricted expression profiles, or altered expression levels in neoplastic cells relative to their normal counterparts. Comprehensive expression profiling approaches such as the analysis of oligonucleotide- or complementary DNA (cDNA)-microarrays have greatly

enhanced these efforts. Genes and their cognate proteins identified using such methods offer additional diagnostic and therapeutic targets that may aid in the understanding and treatment of prostate carcinoma.

DRUG DESCRIPTORS:
*prostate specific antigen; *acid phosphatase prostate isoenzyme; *prostate specific membrane antigen; *proteinase
tumor vaccine--drug development--dv; tumor vaccine--pharmacology--pd; oligonucleotide; complementary DNA; gene product; granulocyte macrophage colony stimulating factor; serotonin receptor; transcription factor E2F; transcription factor; protein p53; unclassified drug
MEDICAL DESCRIPTORS:
*prostate carcinoma--diagnosis--di; *prostate carcinoma--etiology--et; *gene targeting
adoptive immunotherapy; early diagnosis; drug targeting; cancer diagnosis; gene therapy; cancer genetics; carcinogenesis; DNA microarray; dendritic cell; protein localization; oncogene neu; cell specificity; human; nonhuman; conference paper
DRUG TERMS (UNCONTROLLED): protein her 2; hepsin; transcription factor 5
CAS REGISTRY NO.: 9001-92-7 (proteinase)
SECTION HEADINGS:
016 Cancer
022 Human Genetics
026 Immunology, Serology and Transplantation
028 Urology and Nephrology
037 Drug Literature Index

7/9/9 **(Item 3 from file: 73)**
DIALOG(R)File 73:EMBASE

11336092 EMBASE No: 2001350575
Integrating DNA and tissue microarrays cancer profiling
Ibarrola N.; Pandey A.
AUTHOR EMAIL: nibarrola@bmb.sdu.dk
Trends in Biochemical Sciences (TRENDS BIOCHEM. SCI.) (United Kingdom)
01 OCT 2001, 26/10 (589)
CODEN: TBSCD ISSN: 0968-0004
DOCUMENT TYPE: Journal ; Note
LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 1
DRUG DESCRIPTORS:
*DNA
messenger RNA; tumor marker; complementary DNA; prostate specific antigen --endogenous compound--ec; serine proteinase; protein; protein serine threonine kinase; protein antibody; proteome; biological marker; unclassified drug
MEDICAL DESCRIPTORS:
*cancer diagnosis; *DNA microarray; *B cell lymphoma--diagnosis--di; *acute leukemia--diagnosis--di; *prostate cancer--diagnosis--di
prognosis; cancer therapy; gene expression; cancer cell culture; prostate hypertrophy; cancer localization; blood level; cancer epidemiology; gene control; immunohistochemistry; genetic code; protein expression; human; note; priority journal
DRUG TERMS (UNCONTROLLED): protein hepsin; protein pim 1
CAS REGISTRY NO.: 9007-49-2 (DNA); 37259-58-8 (serine proteinase); 67254-75-5 (protein)
SECTION HEADINGS:
016 Cancer

028 Urology and Nephrology
029 Clinical and Experimental Biochemistry

7/9/10 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

06192516 EMBASE No: 1995220804
Hepsin
Kurachi K.; Torres-Rosado A.; Tsuji A.
Department of Human Genetics, Michigan University Medical School,Ann Arbor, MI 48109 United States
Methods in Enzymology (METHODS ENZYMOL.) (United States) 1994, 244/-(100-114)
CODEN: MENZA ISSN: 0076-6879
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH
DRUG DESCRIPTORS:
*complementary dna--endogenous compound--ec; *hydroxyurea; *oligonucleotide ; *polyclonal antibody; *serine proteinase--endogenous compound--ec immunoglobulin g; thymidine; unclassified drug
MEDICAL DESCRIPTORS:
*enzyme analysis
amino acid sequence; animal cell; article; cell cycle; cell strain bhk; cellular distribution; controlled study; enzyme localization; enzyme specificity; enzyme structure; gene expression; hepatoma cell; human; human cell; nonhuman; nucleotide sequence; priority journal; tissue distribution
DRUG TERMS (UNCONTROLLED): hepsin--endogenous compound--ec
CAS REGISTRY NO.: 127-07-1 (hydroxyurea); 37259-58-8 (serine proteinase); 97794-27-9 (immunoglobulin g); 50-89-5 (thymidine)
SECTION HEADINGS:
029 Clinical and Experimental Biochemistry

7/9/11 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

14731358 Genuine Article#: 002FY Number of References: 98
Title: Antibody-based therapeutics: Focus on prostate cancer
Author(s): Ross JS (REPRINT) ; Gray KE; Webb IJ; Gray GS; Rolfe M; Schenkein DP; Nanus DM; Millowsky MI; Bander NH
Corporate Source: Millennium Pharmaceut Inc,Cambridge//MA/ (REPRINT); Millennium Pharmaceut Inc,Cambridge//MA/; Albany Med Coll,Dept Pathol & Lab Med,Albany//NY/12208; Veridex Corp,Raritan//NJ/; Cornell Univ,Weil Coll Med,New York//NY/; New York Presbyterian Hosp,New York//NY/(rossj@mail.amc.edu)
Journal: CANCER AND METASTASIS REVIEWS, 2005, V24, N4 (DEC), P521-537
ISSN: 0167-7659 Publication date: 20051200
Publisher: SPRINGER, VAN GODEWIJCKSTRAAT 30, 3311 GZ DORDRECHT, NETHERLANDS
Language: English Document Type: REVIEW
Geographic Location: USA
Journal Subject Category: ONCOLOGY
Abstract: The recent clinical and commercial success of anti-cancer antibodies such as rituximab, trastuzumab, cetuximab and bevacizumab has continued to foster great interest in antibody-based therapeutics for the treatment of both hematopoietic malignancies and solid tumors. Given the likely lower toxicity for antibodies which, in contrast with traditional cytotoxic small molecule drugs, target tumor cells and have

a lower impact on non-malignant by-stander organs, the potential increases in efficacy associated with conjugation to radioisotopes and other cellular toxins and the ability to characterize the target with clinical laboratory diagnostics to improve the drugs clinical performance, it is anticipated that current and future antibody therapeutics will find substantial roles alone and in combination therapy strategies for the treatment of patients with cancer. A significant number of cell surface proteins, glycoproteins, receptors, enzymes and peptides have been discovered that have become targets for the treatment of advanced hormone-refractory prostate cancer. A variety of naked antibodies and antibody conjugates have currently progressed through preclinical development and are in early or more advanced stages of clinical development. Clinicians, scientists and prostate cancer patients are all keenly interested to learn whether these agents when administered alone or in combination with other hormonal-based and cytotoxic therapies will show lasting benefit for sufferers of this common disease.

Descriptors--Author Keywords: antibody therapeutics ; prostate cancer ; review ; trastuzumab ; bevacizumab ; cetuximab ; PSMA ; PSCA ; hepsin ; MUC1 ; EGFR

Identifiers--KeyWord Plus(R): STEM-CELL ANTIGEN; ENDOTHELIAL GROWTH-FACTOR; RADIOLABELED MONOCLONAL-ANTIBODIES; PHASE-II TRIAL; MEMBRANE ANTIGEN; RADICAL PROSTATECTOMY; EXTRACELLULAR DOMAIN; PATHOLOGICAL STAGE; BREAST-CANCER; EXPRESSION

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    WRIGHT GL, 1995, V1, P18, UROL ONCOL
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FULL ESTIMATED COST                                     39.74       39.95

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=> s (hepsin and (antibody or immunoglobulin))
L6          83 (HEPSIN AND (ANTIBODY OR IMMUNOGLOBULIN))

=> s (hepsin and (modification or variant or variation))
L7          25 (HEPSIN AND (MODIFICATION OR VARIANT OR VARIATION))

=> s l6 and l7
L8          11 L6 AND L7

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=> d l9 bib abs 1-10

L9   ANSWER 1 OF 10  CAPLUS  COPYRIGHT 2006 ACS on STN
AN   2005:1042277  CAPLUS
DN   143:353281
TI   Variants of heterooligomeric microbial toxins with novel cell
     targeting and proteolytic activation behavior for therapeutic use
IN   Leppla, Stephen H.; Liu, Shi-Hui; Bugge, Thomas H.
PA   The Government of the United States, as Represented by the Secretary of
     Health and Human Services, USA
SO   PCT Int. Appl., 83 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
PI   WO 2005090393        A2    20050929    WO 2005-US4216         20050209
     WO 2005090393        A3    20060608
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM,
             SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
```

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005255083 A1 20051117 US 2005-55557 20050209

PRAI US 2004-543417P P 20040209

AB Methods of modifying heterooligomeric bacterial toxins for therapeutic use are described. The methods involve two **modifications** of which one is substituting the targeting domain of the target binding subunit to give it a novel cell- or tissue-specificity. The second **modification** involves changing the proteinase cleavage site of one of the subunits to make it activatable by a novel proteinase, such as one found in the target tissue. In the case of anthrax toxin, where the protective antigen forms a heptamer, more than one **variant** with a different activation cleavage site can be used. This would limit the formation of the active heptamer to tissues where all the necessary proteinases are present. The development of **variants** of protective antigen requiring proteolytic activation by a matrix metalloproteinase, urokinase, or furin is demonstrated. Use of these **variants** in combination to create a heptamer capable of binding lethal factor and killing host cells is demonstrated.

L9 ANSWER 2 OF 10 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN

AN 2005-31394 BIOTECHDS

TI New peptides related to **hepsin** protease protein subfamily useful for treating disorders associated with abnormal expression of protease protein in liver, prostate, T cells from T cell leukemia, or lung tumor;
involving vector-mediated gene transfer and expression in host cell for gene therapy, pharmacogenetics and transgenic animal model construction

AU GAN W; YE J; DI FRANCESCO V; BEASLEY E M

PA APPLERA CORP

PI US 2005250154 10 Nov 2005

AI US 2005-182752 18 Jul 2005

PRAI US 2005-182752 18 Jul 2005; US 2001-820002 29 Mar 2001

DT Patent

LA English

OS WPI: 2005-758012 [77]

AN 2005-31394 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - An isolated peptide (I), is new.

DETAILED DESCRIPTION - The isolated peptide (I) comprises: (a) a fully defined sequence of 376 amino acids (P1), given in the specification; (b) an allelic **variant** or ortholog of (a), which is encoded by a nucleic acid molecule that hybridizes under stringent conditions to the opposite strand of the nucleic acid molecule comprising a fully defined sequence of 1615 (S1) or 21784 (S2) bp, given in the specification; or (c) a fragment of (a) comprising at least 10 contiguous amino acids. INDEPENDENT CLAIMS are also included for: (1) an isolated **antibody** that selectively binds to (I); (2) an isolated nucleic acid molecule (II) comprising a sequence encoding (I), or its complement; (3) a gene chip comprising (II); (4) a transgenic non-human animal comprising (II); (5) a nucleic acid vector comprising (II); (6) a host cell containing the vector in (5); (7) producing (I), comprising: (a) introducing a nucleotide sequence encoding the amino acid sequence of (I) into a host cell; and (b) culturing the host cell under conditions suitable for the expression of the peptide from the nucleotide sequence; (8) detecting the presence of (I) in a sample, comprising contacting the sample with a detection agent that specifically allows detection of the presence of the peptide in the sample then detecting the presence of the peptide; (9) detecting the presence of (II) in a sample, comprising: (a) contacting the sample with an oligonucleotide that hybridizes to (II)

under stringent conditions; and (b) determining whether the oligonucleotide binds to (II) in the sample; (10) identifying a modulator of (I) or its expression, comprising contacting (I) or a cell expressing (I) with an agent and determining if the agent modulated the function or activity, or expression of the peptide; (11) identifying an agent that binds to (I), comprising contacting the peptide with an agent and assaying the contacted mixture to determine whether a complex is formed with the agent bound to the peptide; (12) a pharmaceutical composition comprising the agent identified in (11) and a carrier; (13) treating a disease or condition mediated by human protease protein, comprising administering to a patient the agent identified in (11); (14) an isolated human protease comprising a sequence that is at least 70 % identical to a (P1); (15) an isolated nucleic acid molecule encoding a human secreted peptide, which is at least 80 % identical to (S1) or (S2).

BIOTECHNOLOGY - Preferred Method: Identifying a modulator of (I) comprises administration of the agent to a host cell containing the vector that expresses (I). Preferred Peptide: The human secreted peptide is preferably 90 % identical to (P1). Preferred Nucleic Acid: The nucleic acid molecule in (15) is preferably 90 % identical to (S1) or (S2).

ACTIVITY - Cytostatic. No biological data given.

MECHANISM OF ACTION - Gene therapy.

USE - The peptides are useful in substantial and specific assays related to functional information of the peptide sequences, to raise **antibodies** or to elicit immune response, as reagents in assays to determine the levels of protein in biological fluids, and as markers for tissues where the corresponding protein is expressed. The peptides and **antibodies** are useful in drug screening assays, tissue typing and pharmacogenomic analysis. They are also useful in treating disorders associated with the absence of, inappropriate, or unwanted expression of protease protein in liver, prostate, T cells from T cell leukemia, hepatocellular carcinoma, or lung tumor. The nucleic acid molecules are useful for probes, primers and chemical intermediates in biological assays, for constructing recombinant vectors, expressing antigenic portions of the protein. The peptide and nucleic acid sequences are useful as models for the development of human therapeutic targets, aid in the identification of therapeutic proteins and serve as targets for the development of human therapeutic agents that modulate protease activity in cells and tissues that express the protease peptide. The host cells are useful in producing a protease protein or peptide, and non-human transgenic animals.

EXAMPLE - No example given.(55 pages)

L9 ANSWER 3 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:333822 CAPLUS
DN 140:352647
TI Modified **hepsin** zymogens having a substitute activation sequence and their use for improved **hepsin** production and the production of anti-**hepsin antibodies**
IN Parry, Gordon; Vogel, David; Whitlow, Marc; Wu, Qingyu
PA Schering Aktiengesellschaft, Germany
SO PCT Int. Appl., 160 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004033630	A2	20040422	WO 2003-US31219	20031002
	WO 2004033630	A3	20050210		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,

recombinant protein production for use in disease therapy and gene therapy

AU XIAO Y
PA BAYER HEALTHCARE AG
PI WO 2004009803 29 Jan 2004
AI WO 2003-EP7958 22 Jul 2003
PRAI US 2003-459976 4 Apr 2003; US 2002-397614 23 Jul 2002
DT Patent
LA English
OS WPI: 2004-132961 [13]
AN 2004-08544 BIOTECHDS
AB DERWENT ABSTRACT:

NOVELTY - An isolated **hepsin** polynucleotide (I) which encodes a **hepsin** polypeptide having a sequence of 476 (P1) amino acids and which comprises a sequence of 1769 (S1) bp, fully defined in the specification, is new.

DETAILED DESCRIPTION - An isolated **hepsin** polynucleotide (I) which: (a) encodes a **hepsin** polypeptide having a sequence of 476 (P1) amino acids or a sequence at least 50% identical to P1; (b) comprises a sequence of 1769 (S1) bp, fully defined in the specification; (c) hybridizes under stringent conditions to (a) or (b); (d) deviates from (a)-(c) due to the degeneration of the genetic code; or (e) is a fragment, derivative or allelic **variant** of (a)-(d). INDEPENDENT CLAIMS are also included for the following: (1) an expression vector comprising (I); (2) a host cell containing the expression vector; (3) a substantially purified **hepsin** polypeptide; (4) a method for producing **hepsin** polypeptide; (5) a method for detecting (I), and/or **hepsin** polypeptide; (6) a diagnostic kit for conducting the method cited above; (7) a method of screening for agents that decrease or regulate the activity of **hepsin**; (8) a method of reducing the activity of **hepsin**; (9) a reagent that modulates the activity of (I) or the **hepsin** polypeptide; and (10) a pharmaceutical composition comprising the expression vector or the reagent and a carrier.

BIOTECHNOLOGY - Preferred Method: Producing the **hepsin** polypeptide comprises culturing the host cell for expression of **hepsin** polypeptide; and recovering the subtilase-like serine protease polypeptide from the host cell culture. Detecting (I) comprises hybridizing (I) to a nucleic acid material of a biological sample to form a hybridization complex; and detecting the hybridization complex. Before hybridization, the nucleic acid material of the biological sample is amplified. Detecting (I) or polypeptide comprises contacting a biological sample with a reagent that specifically interacts to (I) or the polypeptide; and detecting the interaction. Screening for agents that decrease the activity of **hepsin** comprises contacting a test compound with (I) or **hepsin** polypeptide; and detecting binding of the test compound to (I) or **hepsin** polypeptide, where a test compound that binds to the polypeptide or polynucleotide is identified as a potential therapeutic agent for decreasing the activity of **hepsin**. Screening for agents that regulate the activity of **hepsin** comprises contacting a test compound with (I) or **hepsin** polypeptide; and detecting a **hepsin** activity of the polypeptide, where a test compound that increases or decreases the activity is identified as a potential agent for increasing or decreasing **hepsin** activity of the polypeptide, respectively. Reducing the activity of **hepsin** comprises contacting a cell with a reagent that specifically binds to (I) and/or **hepsin** polypeptide, where the activity of **hepsin** is reduced.

ACTIVITY - Cardiant; Antiinflammatory; Hemostatic; Antidiabetic; Nootropic; Neuroprotective; Hepatotropic. No biological data given.

MECHANISM OF ACTION - **Hepsin** inhibitor.

USE - The polypeptides, polynucleotide expression vector and reagent are useful for the preparation of a medicament for modulating the activity of a **hepsin** in a disease, such as a cardiovascular,

TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU	2003279754	A1	20040504	AU 2003-279754	20031002
US	2004132156	A1	20040708	US 2003-678816	20031002
EP	1558731	A2	20050803	EP 2003-773093	20031002

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK

JP	2006507813	T2	20060309	JP 2004-543082	20031002
PRAI US	2002-416038P	P	20021004		
	WO 2003-US31219	W	20031002		

AB The physiol. activator activator of **hepsin** is unknown and the activated form of the naturally occurring **hepsin** mols are short-lived, making it difficult to produce anti-**hepsin antibodies**. Thus, a modified zymogen of human **hepsin** is generated where the wild-type activation sequence RIVGG at positions 162-166 is replaced with DDDDKIVGG, an enterokinase cleavage site. The modified **hepsin** mols. are cleaved at the substitute activation sequence, thereby generating activated modified **hepsin** mol., or fragments or derivs. thereof, that exhibit the functional activity of naturally occurring, wild-type **hepsin** mols. The modified **hepsin** mols. of the invention are stable and can be used to produce anti-**hepsin antibodies** that recognize both modified and wild-type **hepsin** mols.

L9 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:119871 CAPLUS
DN 140:158535
TI Gene expression profiling of Gleason grades 3 and 4/5 prostate cancer for identifying tumor markers, and diagnostic and therapeutic uses
IN Mahadevappa, Mamatha; Zhang, Zhaomei; Warrington, Janet A.; Palma, John F.; Caldwell, Mitchell C.; Chen, Zuxiong; Fan, Zhenbin; Mcneal, John E.; Nolley, Rosalie; Stamey, Thomas A.
PA Affymetrix, Inc., USA
SO U.S. Pat. Appl. Publ., 40 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004029151	A1	20040212	US 2003-411537	20030409
	US 2005272052	A1	20051208	US 2004-975592	20041027
PRAI	US 2002-371304P	P	20020409		
	US 2003-411537	A2	20030409		

AB Many genes are affected in prostate cancers which have not been previously identified. This includes genes that have been up-regulated or down-regulated. Monitoring the expression levels of these genes is useful to identify the existence of prostate cancer. Down-regulated and up-regulated genes have been identified in Gleason grades 3 and 4/5 cancer, using the gene profile from benign prostatic hyperplasia (BPH) as control tissue. **Hepsin** appears to be the most promising, as its mRNA was highly up-regulated in neoplastic prostate tissue. The regulated genes can be used diagnostically, prognostically, therapeutically, and for drug screening.

L9 ANSWER 5 OF 10 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2004-08544 BIOTECHDS
TI New polynucleotide encoding a **hepsin** polypeptide, useful for treating diseases associated with hydroxylase dysfunction, e.g. cardiovascular disorder, cancer, inflammatory disease, or respiratory disease;

endocrinological, hormonal, metabolic (including diabetes), inflammatory, gastrointestinal, liver, hematological, respiratory, neurological, reproductive or genitourinary disorders (claimed). The polypeptides may also be used to identify compounds which may act as activators or inhibitors at the enzyme's active site, to raise specific **antibodies** which can block the enzyme and effectively reduce its activity, as a bait protein in a two-hybrid or three-hybrid assay to identify other proteins which bind to or interact with the human **hepsin** polypeptide and modulate its activity, and for immunization of mammals.

ADMINISTRATION - Dosage is 0.1-100000 micrograms, up to a total dose of about 1 g. Administration can be oral, intravenous, intramuscular, intra-arterial, intramedullary, intrathecal, intraventricular, transdermal, subcutaneous, intraperitoneal, intranasal, parenteral, topical, sublingual or rectal.

EXAMPLE - Pichia pastoris expression vector pPICZB was used to produce large quantities of recombinant human subtilase-like serine protease polypeptides in yeast. The ACAD-encoding DNA was derived from a defined 2248- or 1820-bp sequence. Before insertion into pPICZB, the DNA sequence was modified in such a way that it contained at its 5'-end an initiation codon and at its 3'-end an enterokinase cleavage site, a His6 reporter tag, and a termination codon. Recognition sequences for restriction endonucleases were added at both termini and after digestion of the multiple cloning site of pPICZB, the modified DNA sequence was ligated into pPICZB. The resulting pPICZ/md-His6 vector was used to transform yeast. Yeast was cultivated in 5L shake flasks, and recombinantly produced protein was isolated from the culture by affinity chromatography in the presence of 8M urea. Separation of the polypeptide from the His6 reporter tag was done by site-specific proteolysis using enterokinase, which obtained human **hepsin** polypeptide.(136 pages)

L9 ANSWER 6 OF 10 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2004-21375 BIOTECHDS
TI Vaccinating an individual against **hepsin** by inoculation with a **hepsin** peptide that elicits an immune response, useful in diagnosing or treating cancer, such as ovarian, lung, prostate and colon cancer;
hepsin protein and antisense sequence for use in disease therapy and gene therapy
AU O'BRIEN T J; CANNON M J; SANTIN A; BEARD J; SHIGEMASA K
PA O'BRIEN T J; CANNON M J; SANTIN A; BEARD J; SHIGEMASA K
PI US 2004166117 26 Aug 2004
AI US 2003-652993 29 Aug 2003
PRAI US 2003-652993 29 Aug 2003; US 2000-510738 22 Feb 2000
DT Patent
LA English
OS WPI: 2004-603979 [58]
AN 2004-21375 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Vaccinating an individual against **hepsin** comprises inoculating an individual with a **hepsin** peptide that elicits an immune response in the individual, and vaccinating the individual against **hepsin**.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) a method of producing immune-activated cells directed toward **hepsin**, comprising exposing immune cells to a **hepsin** protein or its fragment, where the exposure to the **hepsin** protein or its fragment activates the immune cells, thereby producing immune-activated cells directed toward **hepsin**; (2) a method of immunotherapy targeted toward **hepsin** in an individual, comprising isolating dendritic cells from the individual, expressing a **hepsin** protein or its fragment in the dendritic cells, exposing immune cells comprising T cells isolated from the

individual to the dendritic cells, where the dendritic cells would generate **hepsin**-specific T cells from the immune cells, and transferring the dendritic and/or immune cells back to the individual, where the immune cells would activate **hepsin**-specific immune responses in the individual, thereby generating immunotherapy targeted toward **hepsin** in the individual; (3) a method of monitoring the efficacy of vaccinating an individual with **hepsin** or **hepsin** peptide, comprising vaccinating the individual with the **hepsin** or **hepsin** peptide, isolating T cells from the individual, and measuring immune responses induced by the **hepsin** or **hepsin** peptide, where an increased level of immune responses compared to those exhibited by cells from normal individual indicates that the individual has been vaccinated by the **hepsin** or **hepsin** peptide; (4) a method of inhibiting expression of endogenous **hepsin** in a cell, comprising introducing into the cell a vector comprising a sequence complementary to a fully defined sequence of 1783 bp (SEQ ID NO: 188), where expression of the vector in the cell produces **hepsin** antisense RNA that hybridizes to endogenous **hepsin** mRNA, thereby inhibiting expression of endogenous **hepsin** in the cell; (5) a method of inhibiting **hepsin** protein in a cell, comprising introducing into the cell an **antibody** which is specific for a **hepsin** protein or its fragment, where binding of the **antibody** to the **hepsin** protein inhibits **hepsin** protein in the cell; (6) a method of targeted therapy to an individual, comprising administering a compound to an individual, where the compound has a therapeutic moiety and a targeting moiety specific for **hepsin**; (7) an immunogenic composition comprising a full length **hepsin** protein or a fragment of a **hepsin** protein, and an adjuvant; (8) an oligonucleotide having a sequence complementary to SEQ ID NO: 188; (9) a composition comprising the oligonucleotide of (8) and a carrier; (10) a method of treating a neoplastic state in an individual in need of such treatment, comprising administering to the individual an oligonucleotide of (8); (11) a method of screening for compounds that inhibit **hepsin** activity, comprising contacting a sample comprising **hepsin** protein with a compound, and assaying for **hepsin** protease activity, where a decrease in the **hepsin** protease activity in the presence of the compound relative to **hepsin** protease activity in the absence of the compound indicates the compound inhibits **hepsin** activity; (12) an isolated DNA encoding a **hepsin variant** comprising a fully defined sequence of 72 amino acids (SEQ ID NO: 195) or its fragment; (13) an isolated and purified **hepsin variant** protein, comprising the amino acid sequence of SEQ ID NO: 195 or its fragment; and (14) a method of detecting tumor cells in a sample, comprising detecting the expression of a **hepsin** protein **variant** of (13), where the presence of the **hepsin variant** in the sample indicates that the sample contains tumor cells.

BIOTECHNOLOGY - Preferred Method: The individual in any of the methods cited above has cancer, is suspected of having cancer or is at risk of getting cancer, such as ovarian, lung, prostate and colon cancer. The length of the **hepsin** peptide is 9-20 residues long. The peptide is from any of 20 fully defined sequences of 9 or 20 amino acids. The **hepsin** peptide in vaccinating an individual is in peptide-loaded dendritic cells or is expressed from an expression vector. The immune cells in producing immune-activated cells are B cells, T cells and dendritic cells. The expression of **hepsin** dendritic cells in the method of immunotherapy is obtained by a mean selected from transfection, transduction and loading the dendritic cells with a **hepsin** protein or its fragment. The immune response in monitoring the efficacy of vaccinating an individual is selected from T cell proliferation induced by said **hepsin** or **hepsin** peptide, frequency of cytokine-secreting T cells specific to the **hepsin** or **hepsin** peptide and frequency of T cells

expressing T cell receptor specific to the **hepsin** or **hepsin** peptide. The targeting moiety in the method of (6) is an **antibody** specific for **hepsin** and a ligand or ligand-binding domain that binds **hepsin**. The therapeutic moiety is a radioisotope, a toxin, a chemotherapeutic agent, an immune stimulant or a cytotoxic agent. The detection of **hepsin variant** in detecting tumor cells is performed at DNA or protein level. The tumor cells are ovarian cancer cells, prostate cancer cells or kidney cancer cells.

ACTIVITY - Cytostatic. No biological data given.

MECHANISM OF ACTION - Cathepsin-Inhibitor.

USE - The methods and compositions of the present invention are useful in the fields of molecular biology and medicine, in particular for diagnosing and treating cancer, such as ovarian, lung, prostate and colon cancer.

EXAMPLE - No relevant example given.(85 pages)

L9 ANSWER 7 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:912576 CAPLUS
DN 139:392149
TI Human cDNA sequences and their encoded proteins and diagnostic and therapeutic uses
IN Mezes, Peter D.; Rastelli, Luca; Herrmann, John L.; MacDougall, John R.; Zhong, Haihong; Casman, Stacie J.; Boldog, Ferenc L.; Shimkets, Richard A.; Gorman, Linda; Eisen, Andrew J.; Spaderna, Steven K.; Vernet, Corine A. m.; Berghs, Constance; Spytek, Kimberly A.; Dipippo, Vincent A.; Zerhusen, Bryan D.; Peyman, John A.; Ellerman, Karen; Stone, David J.; Grosse, William M.; Alsobrook, John P.; Lepley, Denise M.; Rieger, Daniel K.; Burgess, Catherine E.; Edinger, Shlomit R.; Voss, Edward Z.; Miller, Charles E.
PA Curagen Corporation, USA
SO U.S. Pat. Appl. Publ., 313 pp., Cont.-in-part of U.S. Ser. No. 44,564.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 167

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003215449	A1	20031120	US 2002-99322	20020315
	US 6964849	B2	20051115		
	US 2004018196	A1	20040129	US 2002-44564	20020111
	US 6991901	B2	20060131		
	US 2003203363	A1	20031030	US 2002-94466	20020307
	CA 2440337	AA	20020919	CA 2002-2440337	20020308
	CA 2440345	AA	20020919	CA 2002-2440345	20020308
	CA 2440108	AA	20021010	CA 2002-2440108	20020308
	EP 1427749	A2	20040616	EP 2002-713788	20020308
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	AU 2005200106	A1	20050210	AU 2005-200106	20050112
	US 2006013813	A1	20060119	US 2005-54281	20050208
	AU 2006201467	A1	20060504	AU 2006-201467	20060407
PRAI	US 2001-261013P	P	20010111		
	US 2001-261014P	P	20010111		
	US 2001-261018P	P	20010111		
	US 2001-261026P	P	20010111		
	US 2001-261029P	P	20010111		
	US 2001-278152P	P	20010323		
	US 2001-313170P	P	20010817		
	US 2001-318410P	P	20010910		
	US 2002-44564	A2	20020111		
	AU 2000-37360	A3	20000309		
	AU 2000-78680	A3	20001006		
	US 2001-274191P	P	20010308		

US 2001-274194P P 20010308
US 2001-274281P P 20010308
US 2001-274322P P 20010308
US 2001-274849P P 20010309
US 2001-275235P P 20010312
US 2001-275578P P 20010313
US 2001-275579P P 20010313
US 2001-275601P P 20010313
US 2001-276000P P 20010314
US 2001-276776P P 20010316
US 2001-276994P P 20010319
US 2001-277239P P 20010320
US 2001-277321P P 20010320
US 2001-277327P P 20010320
US 2001-277338P P 20010320
US 2001-277791P P 20010321
US 2001-277833P P 20010322
US 2001-278894P P 20010326
US 2001-278999P P 20010327
US 2001-279036P P 20010327
US 2001-279344P P 20010328
US 2001-279995P P 20010330
US 2001-280233P P 20010330
US 2001-280802P P 20010402
US 2001-280822P P 20010402
US 2001-280900P P 20010402
US 2001-281194P P 20010404
US 2001-283675P P 20010413
US 2001-287424P P 20010430
US 2001-288052P P 20010502
US 2001-288066P P 20010502
US 2001-288148P P 20010502
US 2001-288228P P 20010502
US 2001-288342P P 20010503
US 2001-288528P P 20010503
US 2001-291190P P 20010515
US 2001-291099P P 20010516
US 2001-291240P P 20010516
US 2001-291766P P 20010517
US 2001-294485P P 20010530
US 2001-294821P P 20010531
US 2001-294889P P 20010531
US 2001-294899P P 20010531
US 2001-296693P P 20010607
US 2001-296856P P 20010608
US 2001-303230P P 20010705
US 2001-303237P P 20010705
US 2001-310913P P 20010808
US 2001-311978P P 20010813
US 2001-312191P P 20010814
US 2001-312916P P 20010816
US 2001-313182P P 20010817
US 2001-313626P P 20010820
US 2001-314018P P 20010821
US 2001-315227P P 20010827
US 2001-318403P P 20010910
US 2001-318510P P 20010910
US 2001-335302P P 20011031
US 2001-338375P P 20011204
US 2002-99322 A1 20020315

AB Disclosed herein are 20 cDNA sequences that encode novel human polypeptides that are members of the following protein families: LIV-1, NRD convertase, kallikrein, multidrug transporter, glucose transporter type 2, Frizzled homolog 9, prominin, and **hepsin**. Twelve of

these sequences (designated SEC1-SEC12) may be useful for diagnosis and treatment of angiogenic-associated disorders. Also disclosed are polypeptides encoded by these nucleic acid sequences, and **antibodies**, which immunospecifically-bind to the polypeptide, as well as derivs., **variants**, mutants, or fragments of the aforementioned polypeptide, polynucleotide, or **antibody**. The invention further discloses therapeutic, diagnostic and research methods for diagnosis, treatment, and prevention of disorders involving any one of these novel human nucleic acids and proteins.

RE.CNT 103 THERE ARE 103 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 8 OF 10 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2004-00793 BIOTECHDS
TI New isolated human protease proteins and genes, useful for developing therapeutic or diagnostic compositions, particularly modulators of **hepsin** protease activity in cells or tissues for treating e.g. inflammation or cancer;
involving vector-mediated gene transfer and expression in host cell for use in therapy
AU GAN W; YE J; FRANCESCO V D; BEASLEY E M
PA APPLERA CORP
PI US 2003129726 10 Jul 2003
AI US 2002-274031 21 Oct 2002
PRAI US 2002-274031 21 Oct 2002; US 2001-820002 29 Mar 2001
DT Patent
LA English
OS WPI: 2003-829569 [77]
AN 2004-00793 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - An isolated human protease peptides comprising a 376 residue amino acid sequence (I), given in the specification, an allelic **variant** or an ortholog of (I), a fragment of (I), which comprises at least 10 contiguous amino acids, or an at least 70 % homolog with (I), is new.

DETAILED DESCRIPTION - An isolated human protease peptides comprising a 376 residue amino acid sequence (I), given in the specification, an allelic **variant** or an ortholog of (I), a fragment of (I), which comprises at least 10 contiguous amino acids, or an at least 70 % homolog with (I), is new. The allelic **variant** or ortholog is encoded by a nucleic acid molecule that hybridizes under stringent conditions to the opposite strand of a DNA having 1615 (II) or 21784 (III) base pair sequences, given in the specification. INDEPENDENT CLAIMS are also included for the following: (1) an isolated **antibody** that selectively binds to the peptide; (2) an isolated nucleic acid molecule consisting of a nucleotide sequence comprising a nucleotide that: (a) encodes (I); (b) is the complement of a nucleotide sequence of (a); or (c) that shares at least 80 % homology with (II) or (III); (3) a gene chip comprising the nucleic acid molecule of (2); (4) a transgenic non-human animal comprising the nucleic acid molecule of (2); (5) a nucleic acid vector comprising the nucleic acid molecule of (2); (6) a host cell containing the vector of (5); (7) producing the novel peptides; (8) detecting the presence of the novel peptide or nucleic acid molecules of (2); (9) identifying a modulator of the novel peptide or of the expression of the peptide; (10) identifying an agent that binds to any of the peptides by contacting the peptide with an agent and assaying the contacted mixture to determine whether a complex is formed with the agent bound to the peptide; (11) a pharmaceutical composition comprising an agent identified by the method of (10) and a pharmaceutical carrier; and (12) treating a disease or condition mediated by a human protease protein comprising administering to a patient the agent identified by the method of (10).

BIOTECHNOLOGY - Preparation (Claimed): Producing the peptide comprises introducing the nucleotide sequence encoding any of the amino

acid sequences into a host cell, and culturing the host cell under conditions in which the peptides are expressed from the nucleotide sequence.Preferred Method: In the method of (8), detecting for the presence of any of the peptides in a sample comprises contacting the sample with a detection agent that specifically allows detection of the presence of the peptide in the sample, and then detecting the presence of the peptide. Detecting the presence of the nucleic acid molecule comprises contacting the sample with an oligonucleotide that hybridizes to the nucleic acid molecule under stringent conditions, and determining whether the oligonucleotide binds to the nucleic acid molecule in the sample. In the method of (9), identifying a modulator of the peptide comprises contacting the peptide with an agent, and determining if the agent has modulated the function or activity of the peptide. The agent is administered to a host cell comprising an expression vector that expresses the peptide. Identifying a modulator of the expression of the peptide comprises contacting a cell expressing the peptide with an agent, and determining if the agent has modulated the expression of the peptide. Preferred Peptide: Preferably, the peptide shares at least 90 % homology with (I). The peptide is preferably encoded by a nucleic acid molecule that shares at least 90 % homology with (II) or (III).

ACTIVITY - Antiinflammatory; Cytostatic; Antiarteriosclerotic. No biological data is given.

MECHANISM OF ACTION - None given.

USE - The human protease peptides and nucleic acid molecules are useful in the development of human therapeutics and diagnostic compositions. These molecules are particularly useful as models for developing human therapeutic targets, identifying therapeutic proteins, or serving as targets for the development of human therapeutic agents that modulate protease activity in cells and tissues that express the protease. The peptides are also useful for raising **antibodies** or eliciting an immune response, as a reagent (including the labeled reagent) in assays designed to quantitatively determine levels of the protein (or its binding partner or ligand) in biological fluids; or as markers for tissues in which the corresponding protein is preferentially expressed. The agents identified are useful for treating protease-related conditions that are specific for the **hepsin** subfamily of proteases, particularly in cells and tissues that express the protease. (All claimed.) The modulator of the peptide is also useful for treating a disorder mediated by a human protease protein (claimed), e.g. inflammation, cancer, arteriosclerosis or degenerative disorders. The vectors and host cells are useful for produce the protease protein or peptide.

EXAMPLE - No example given. (55 pages)

L9 ANSWER 9 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
AN 2002:315100 CAPLUS
DN 136:336302
TI Protein and cDNA sequences for novel human proteins and their use in diagnosis and disease treatment
IN Edinger, Shlomit; Gerlach, Valerie; MacDougall, John R.; Malyankar, Uriel M.; Smithson, Glennda; Millet, Isabelle; Peyman, John A.; Stone, David J.; Gunther, Erik; Ellerman, Karen; Shimkets, Richard A.; Padigaru, Muralidhara; Guo, Xiaojia; Patturajan, Meera; Taupier, Raymond J.; Burgess, Catherine E.; Zerhusen, Bryan D.; Kekuda, Ramesh; Spytek, Kimberly A.; Gangolli, Esha A.; Fernandes, Elma R.; Gorman, Linda
PA Curagen Corporation, USA
SO PCT Int. Appl., 305 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002033087	A2	20020425	WO 2001-US32496	20011017

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

	AU 2002016637	A5	20020429	AU 2002-16637	20011007
	US 2003212256	A1	20031113	US 2001-981151	20011016
PRAI	US 2000-241040P	P	20001017		
	US 2000-241058P	P	20001017		
	US 2000-241063P	P	20001017		
	US 2000-241243P	P	20001017		
	US 2000-242152P	P	20001020		
	US 2000-242482P	P	20001023		
	US 2000-242611P	P	20001023		
	US 2000-242612P	P	20001023		
	US 2000-242880P	P	20001024		
	US 2000-242881P	P	20001024		
	US 2000-259028P	P	20001229		
	US 2001-269813P	P	20010220		
	US 2001-294108P	P	20010425		
	US 2001-286324P	P	20010529		
	US 2001-303698P	P	20010709		
	US 2001-303968P	P	20010709		
	US 2001-981151	A2	20011016		
	WO 2001-US32496	W	20011017		

AB Disclosed herein are 10 nucleic acid sequences that encode novel polypeptides and their **variants**. The polypeptides show sequence homol. to zinc metalloproteases, ADAM-TS7, α2-macroglobulin, ileal sodium/bile acid cotransporter, prohibitin, macrophage stimulating protein, fatty acid-binding protein, gap junction β5 protein, metallothionein, CIP4, **hepsin**/plasma transmembrane protein, and spinesin. Protein domains or motifs, tissue expression profiles, chromosomal mapping, and single nucleotide polymorphisms are provided. Also disclosed are polypeptides encoded by these nucleic acid sequences, and **antibodies**, which immunospecifically-bind to the polypeptide, as well as derivs., **variants**, mutants, or fragments of the aforementioned polypeptide, polynucleotide, or **antibody**. The invention further discloses therapeutic, diagnostic and research methods for diagnosis, treatment, and prevention of disorders involving any one of these novel human nucleic acids and proteins.

L9 ANSWER 10 OF 10 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:539838 CAPLUS
DN 137:74487
TI Human proteins and their cDNA sequences and diagnostic and therapeutic uses
IN Mezes, Peter S.; Rastelli, Luca; Herrmann, John L.; MacDougall, John R.; Zhong, Haihong; Casman, Stacie J.; Boldog, Ferenc; Shimkets, Richard A.; Gorman, Linda; Crasta, Oswald R.; Mysore, Kiran Kumar; Folkerts, Otto; Martin, Gregory B.; Eisen, Andrew; Spaderna, Steven K.; Vernet, Corine A. M.; Bergh, Constance; Spytek, Kimberly A.; Dipippo, Vincent A.; Zerhusen, Bryan D.; Peyman, John A.; Ellerman, Karen; Stone, David J.; Grosse, William M.; Alsobrook, John P., II; Lepley, Denise M.; Rieger, Daniel K.; Burgess, Catherine E.; Edinger, Schlomit
PA Curagen Corporation, USA
SO PCT Int. Appl., 443 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 167

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

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     ---------------      ----   --------    --------------------   --------
PI   WO 2002055705         A2    20020718    WO 2002-US609          20020111
     WO 2002055705         A3    20030410
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA,
             UG, US, UZ, VN, YU, ZA, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB,
             GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA,
             GN, GQ, GW, ML, MR, NE, SN, TD, TG
     CA 2433742            AA    20020718    CA 2002-2433742        20020111
     EP 1358327            A2    20031105    EP 2002-704097         20020111
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2005508133         T2    20050331    JP 2002-556751         20020111
     AU 2005200106         A1    20050210    AU 2005-200106         20050112
     AU 2006201467         A1    20060504    AU 2006-201467         20060407
PRAI US 2001-261013P       P     20010111
     US 2001-261014P       P     20010111
     US 2001-261018P       P     20010111
     US 2001-261026P       P     20010111
     US 2001-261029P       P     20010111
     US 2001-313170P       P     20010817
     US 2001-318410P       P     20010910
     AU 2000-37360         A3    20000309
     AU 2000-78680         A3    20001006
     WO 2002-US609         W     20020111
AB   Disclosed herein are nucleic acid sequences that encode novel
     polypeptides. The cDNAs encoding 12 human proteins associated with
     angiogenic disorders (designated SEC1 to SEC12) and 8 addnl. human
     proteins (designated NOV1 to NOV8) are provided. Chromosomal map
     locations, tissue typing, domain anal., and single nucleotide
     polymorphisms are also provided. Also disclosed are polypeptides encoded
     by these nucleic acid sequences, and antibodies, which
     immunospecifically-bind to the polypeptide, as well as derivs.,
     variants, mutants, or fragments of the aforementioned polypeptide,
     polynucleotide, or antibody. The invention further discloses
     therapeutic, diagnostic and research methods for diagnosis, treatment, and
     prevention of disorders involving any one of these novel human nucleic
     acids and proteins.


=> d his

     (FILE 'HOME' ENTERED AT 14:51:34 ON 27 JUN 2006)

     FILE 'CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIOBASE' ENTERED AT
     14:52:01 ON 27 JUN 2006
L1            79 S HEPSIN AND ANTIBODY
L2             2 S (MODIFIED HEPSIN)
L3             1 S (HEPSIN VARIANT)
L4             1 S L1 AND L3
L5             1 DUPLICATE REMOVE L2 (1 DUPLICATE REMOVED)

     FILE 'CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIOBASE' ENTERED AT
     15:05:22 ON 27 JUN 2006
L6            83 S (HEPSIN AND (ANTIBODY OR IMMUNOGLOBULIN))
L7            25 S (HEPSIN AND (MODIFICATION OR VARIANT OR VARIATION))
L8            11 S L6 AND L7
L9            10 DUPLICATE REMOVE L8 (1 DUPLICATE REMOVED)
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=> s ((modified hepsin) and antibody)
L10          2 ((MODIFIED HEPSIN) AND ANTIBODY)

=> duplicate remove l10
DUPLICATE PREFERENCE IS 'CAPLUS, BIOTECHDS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L10
L11           1 DUPLICATE REMOVE L10 (1 DUPLICATE REMOVED)

=> d l11 bib abs 1

L11  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2006 ACS on STN  DUPLICATE 1
AN   2004:333822  CAPLUS
DN   140:352647
TI   Modified hepsin zymogens having a substitute
     activation sequence and their use for improved hepsin production and the
     production of anti-hepsin antibodies
IN   Parry, Gordon; Vogel, David; Whitlow, Marc; Wu, Qingyu
PA   Schering Aktiengesellschaft, Germany
SO   PCT Int. Appl., 160 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
FAN.CNT 1
     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
PI   WO 2004033630         A2    20040422    WO 2003-US31219         20031002
     WO 2004033630         A3    20050210
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
             PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN,
             TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     AU 2003279754         A1    20040504    AU 2003-279754          20031002
     US 2004132156         A1    20040708    US 2003-678816          20031002
     EP 1558731            A2    20050803    EP 2003-773093          20031002
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
     JP 2006507813         T2    20060309    JP 2004-543082          20031002
PRAI US 2002-416038P       P     20021004
     WO 2003-US31219       W     20031002
AB   The physiol. activator activator of hepsin is unknown and the activated
     form of the naturally occurring hepsin mols are short-lived, making it
     difficult to produce anti-hepsin antibodies. Thus, a modified
     zymogen of human hepsin is generated where the wild-type activation
     sequence RIVGG at positions 162-166 is replaced with DDDDKIVGG, an
     enterokinase cleavage site. The modified hepsin mols.
     are cleaved at the substitute activation sequence, thereby generating
     activated modified hepsin mol., or fragments or
     derivs. thereof, that exhibit the functional activity of naturally
     occurring, wild-type hepsin mols. The modified hepsin
     mols. of the invention are stable and can be used to produce anti-hepsin
     antibodies that recognize both modified and wild-type hepsin mols.


=> s ((hepsin peptide)and (antibody or immunoglobulin))
L12          7 ((HEPSIN PEPTIDE) AND (ANTIBODY OR IMMUNOGLOBULIN))

=> duplicate remove l12
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DUPLICATE PREFERENCE IS 'CAPLUS, BIOTECHDS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n
PROCESSING COMPLETED FOR L12
L13 6 DUPLICATE REMOVE L12 (1 DUPLICATE REMOVED)

=> d l13 bib abs 1-6

L13 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
AN 2004:701591 CAPLUS
DN 141:219982
TI Protein and cDNA sequences of human hepsin and their uses in early diagnosis and immunotherapy of ovarian cancer
IN O'Brien, Timothy J.; Cannon, Martin J.; Santin, Alessandro; Beard, John; Shigemasa, Kazushi
PA USA
SO U.S. Pat. Appl. Publ., 85 pp., Cont.-in-part of U.S. Ser. No.. 135,795.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 15

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2004166117	A1	20040826	US 2003-652993	20030829
	US 6268165	B1	20010731	US 2000-510738	20000222
	US 6518028	B1	20030211	US 2001-861966	20010521
	US 2002150908	A1	20021017	US 2001-919048	20010730
	US 6787354	B2	20040907		
	US 2003027181	A1	20030206	US 2002-102283	20020320
	US 6875609	B2	20050405		
	US 2003077618	A1	20030424	US 2002-135795	20020430
	WO 2005021582	A2	20050310	WO 2004-US28234	20040830
	WO 2005021582	A3	20060427		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1658307	A2	20060524	EP 2004-782668	20040830
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
PRAI	US 2000-510738	A3	20000222		
	US 2001-861966	A2	20010521		
	US 2001-919048	A2	20010730		
	US 2002-102283	A2	20020320		
	US 2002-135795	A2	20020430		
	US 1997-41404P	P	19970319		
	US 1998-39211	A2	19980314		
	US 2003-652993	A	20030829		
	WO 2004-US28234	W	20040830		

AB The present invention discloses the hepsin is specifically over-expressed in ovarian and other malignancies. The invention provides the protein and cDNA sequences of human hepsin. A number of **hepsin peptides** can induce immune responses to hepsin, thereby demonstrating the potential of these peptides in monitoring and the development of immunotherapies for ovarian and other malignancies. The invention provides methods of vaccinating an individual against hepsin or produce immune-activated cells directed toward hepsin by inoculating an individual with an expression vector encoding a hepsin protein or a

fragment thereof. The invention also provides methods of inhibiting expression of hepsin in a cell by introducing into a cell a vector encoding an antisense hepsin RNA or an **antibody** that binds the hepsin protein. The genes which are clearly overexpressed include the serine proteases hepsin, stratum corneum chymotrypsin enzyme (SCCE), protease M TADG12, TADG14 and the metalloprotease PUMP-1 protease.

L13 ANSWER 2 OF 6 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2004-21384 BIOTECHDS
TI Use of stratum corneum chymotrytic enzyme (SCCE) peptides, for vaccinating an individual against SCCE, and in monitoring and developing immunotherapies for ovarian and other malignancies;
enzyme peptide and antisense sequence for use in disease therapy and gene therapy
AU O'BRIEN T J; CANNON M J; SANTIN A
PA UNIV ARKANSAS
PI WO 2004075723 10 Sep 2004
AI WO 2004-US5134 20 Feb 2004
PRAI US 2003-372521 21 Feb 2003; US 2003-372521 21 Feb 2003
DT Patent
LA English
OS WPI: 2004-653294 [63]
AN 2004-21384 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - Vaccinating an individual against stratum corneum chymotrytic enzyme (SCCE) comprises inoculating an individual with a SCCE peptide, which elicits an immune response in the individual.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for: (1) producing immune-activated cells directed SCCE; (2) immunotherapy targeted toward SCCE in an individual; (3) monitoring the efficacy of vaccinating an individual with SCCE or SCCE peptide; (4) inhibiting expression of endogenous SCCE in a cell comprising introducing into the cell a vector comprising a sequence complementary to a 969-bp sequence given in the specification (SEQ ID NO: 30), where expression of the vector in the cell produces SCCE antisense RNA that hybridizes to endogenous SCCE mRNA; (5) inhibiting SCCE protein in a cell; (6) targeted therapy to an individual; (7) an immunogenic composition, comprising an immunogenic fragment of SCCE protein and an adjuvant; (8) an oligonucleotide having a sequence complementary to SEQ ID NO: 30; (9) a composition comprising the oligonucleotide of (8) and a physiological carrier; (10) treating a neoplastic state in an individual by administering to the oligonucleotide of (8); and (11) screening for compounds that inhibit SCCE activity.

BIOTECHNOLOGY - Preferred Peptide: The SCCE peptide is in peptide-loaded dendritic cells or is expressed from an expression vector. The length of the **hepsin peptide** is from about 9-20 residues long. The peptide comprises the amino acid sequence: Lys-Met-Asn-Glu-Tyr-Thr-Val-His-Leu SEQ ID NO: 31; Arg-Leu-Ser-Ser-Met-Val-Lys-Lys-Val SEQ ID NO: 32; Leu-Leu-Leu-Pro-Leu-Gln-Ile-Leu-Leu SEQ ID NO: 33; Val-Leu-Val-Asn-Glu-Arg-Trp-Val-Leu SEQ ID NO: 34; Leu-Leu-Pro-Leu-Gln-Ile-Leu-Leu-Leu SEQ ID NO: 35; Ser-Leu-Leu-Leu-Pro-Leu-Gln-Ile-Leu SEQ ID NO: 36; Gly-Pro-Leu-Val-Cys-Arg-Gly-Thr-Leu SEQ ID NO: 80; Met-Ala-Arg-Ser-Leu-Leu-Leu-Pro-Leu SEQ ID NO: 86; or Gln-Arg-Ile-Lys-Ala-Ser-Lys-Ser-Phe SEQ ID NO: 99. Preferred Method: Producing immune-activated cells directed toward SCCE comprises exposing immune cells to a SCCE protein or its fragment, where the exposure to the SCCE protein or fragment activates the immune cells, thereby producing immune-activated cells directed toward SCCE. The immune cells are selected from B cells, T cells and dendritic cells. The length of the SCCE fragment is from about 9-20 residues long. The 9-residue fragment is selected from SED ID NOS: 31, 32, 33, 34, 35, 36, 80, 86 and 99. The dendritic cells are isolated from an individual prior to the exposure, where the activated dendritic cells are reintroduced into the individual subsequent to the exposure. The individual has a cancer, is suspected of

having a cancer or is at risk of getting a cancer, including ovarian, lung, prostate, pancreatic and colon cancer. A method of immunotherapy targeted toward SCCE in an individual comprises isolating dendritic cells from the individual, expressing a SCCE protein or fragment in the dendritic cells, and transferring the dendritic cells back to the individual, where the dendritic cells would activate SCCE-specific immune responses in the individual and generate immunotherapy targeted toward SCCE in the individual. The expression of SCCE in the dendritic cells is obtained by transfection, transduction or loading of the dendritic cells with a SCCE protein or its fragment. Alternatively, the method comprises exposing immune cells comprising T cells isolated from the individual to the dendritic cells, where the dendritic cells would generate SCCE-specific T cells from the immune cells, and transferring the immune cells back to the individual, where the immune cells would activate SCCE-specific immune responses in the individual, and generate immunotherapy targeted toward SCCE in the individual. The targeted therapy may also comprise administering a compound to an individual, where the compound has a therapeutic moiety and a targeting moiety specific for SCCE. The targeting moiety is selected from an **antibody** specific for SCCE, and a ligand or ligand-binding domain that binds SCCE. The therapeutic moiety is selected from a radioisotope, a toxin, a chemotherapeutic agent, an immune stimulant and a cytotoxic agent. Monitoring the efficacy of vaccinating an individual with SCCE or SCCE peptide comprises vaccinating the individual with the SCCE or SCCE peptide, isolating T cells from the individual, and measuring immune responses induced by the SCCE or SCCE peptide, where an increased level of immune responses compared to those exhibited by cells from normal individual indicates that the individual has been vaccinated by the SCCE or SCCE peptide. The immune response may be T cell proliferation induced by the SCCE or SCCE peptide, or frequency of cytokine-secreting T cells specific to the SCCE or SCCE peptide and frequency of T cells expressing T cell receptor specific to the SCCE or SCCE peptide. Inhibiting SCCE in a cell comprises introducing into the cell an **antibody** specific for a SCCE protein or its fragment, where binding of the **antibody** to the SCCE protein inhibits the SCCE protein in the cell. Screening for compounds that inhibit SCCE comprises contacting a sample comprising stratum corneum chymotrytic enzyme protein with a compound, and assaying for SCCE protease activity, where a decrease in the SCCE protease activity in the presence of the compound relative to SCCE protease activity in the absence of the compound indicates that the compound inhibits SCCE activity.

ACTIVITY - Cancer. No biological data given.

MECHANISM OF ACTION - Vaccine; Stratum Corneum Chymotrytic Enzyme Inhibitor.

USE - The SCCE peptide is useful for vaccinating an individual against SCCE, particularly an individual having, suspected or at risk of getting ovarian, lung, prostate, pancreatic or colon cancer. The oligonucleotide is useful for treating a neoplastic state in an individual, such as ovarian, breast, lung, colon, prostate, or pancreatic cancer, and other cancers in which SCCE is overexpressed (all claimed). The peptides are also useful in the monitoring and development of immunotherapies for ovarian and other malignancies. (117 pages)

L13 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:950450 CAPLUS
DN 140:19794
TI Methods for the early diagnosis of ovarian cancer by determining expression of stratum corneum chymotryptic enzyme (SCCE)
IN O'Brien, Timothy J.; Cannon, Martin J.; Santin, Alessandro
PA USA
SO U.S. Pat. Appl. Publ., 61 pp., Cont.-in-part of U.S. Ser. No. 918,243.
CODEN: USXXCO
DT Patent
LA English

FAN.CNT 15

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003223973	A1	20031204	US 2003-372521	20030221
	US 6303318	B1	20011016	US 1998-39211	19980314
	US 6294344	B1	20010925	US 2000-502600	20000211
	US 2002146708	A1	20021010	US 2001-905083	20010713
	US 2002142317	A1	20021003	US 2001-918243	20010730
	US 6627403	B2	20030930		
	CA 2519193	AA	20040910	CA 2004-2519193	20040220
	WO 2004075723	A2	20040910	WO 2004-US5134	20040220
	WO 2004075723	A3	20050310		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	EP 1594989	A2	20051116	EP 2004-713420	20040220
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	US 2004224891	A1	20041111	US 2004-831075	20040423
PRAI	US 1997-41404P	P	19970319		
	US 1998-39211	A2	19980314		
	US 2000-502600	A3	20000211		
	US 2001-905083	A2	20010713		
	US 2001-918243	A2	20010730		
	US 2003-372521	A	20030221		
	WO 2004-US5134	W	20040220		

AB The present invention discloses the protease stratum corneum chymotryptic enzyme (SCCE) is specifically over-expressed in ovarian and other malignancies. A number of SCCE peptides can induce immune responses to SCCE, thereby demonstrating the potential of these peptides in monitoring and the development of immunotherapies for ovarian and other malignancies. The invention provides methods of vaccinating an individual against SCCE or produce immune-activated cells directed toward SCCE by inoculating an individual with an expression vector encoding a SCCE protein or a fragment thereof. The invention also provides methods of inhibiting expression of SCCE in a cell by introducing into a cell a vector encoding an antisense SCCE RNA or an **antibody** that binds the SCCE protein.

L13 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:319344 CAPLUS
DN 138:349663
TI Hepsin protease as a tumor marker, and methods for the early diagnosis and therapy of ovarian cancer and other malignancies
IN O'Brien, Timothy J.; Cannon, Martin J.; Santin, Alessandro
PA USA
SO U.S. Pat. Appl. Publ., 43 pp., Cont.-in-part of U.S. Ser. No. 102,283.
CODEN: USXXCO
DT Patent
LA English

FAN.CNT 15

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003077618	A1	20030424	US 2002-135795	20020430
	US 6268165	B1	20010731	US 2000-510738	20000222
	US 6518028	B1	20030211	US 2001-861966	20010521
	US 2002150908	A1	20021017	US 2001-919048	20010730
	US 6787354	B2	20040907		
	US 2003027181	A1	20030206	US 2002-102283	20020320
	US 6875609	B2	20050405		

	US 2004166117	A1	20040826	US 2003-652993	20030829
PRAI	US 2000-510738	A3	20000222		
	US 2001-861966	A2	20010521		
	US 2001-919048	A2	20010730		
	US 2002-102283	A2	20020320		
	US 1997-41404P	P	19970319		
	US 1998-39211	A2	19980314		
	US 2002-135795	A2	20020430		

AB The disclosed nucleic acid primer sets, used in combination with quant. amplification (PCR) of tissue cDNA, can indicate the presence of specific proteases in a tissue sample. Specifically, the present invention relates to expression of hepsin protease. The detected proteases are themselves specifically over-expressed in certain cancers, and the presence of their genetic precursors may serve for early detection of associated ovarian and other malignancies, and for the design of interactive therapies for cancer treatment. There are provided methods of vaccinating an individual against hepsin or produce immune-activated cells directed toward hepsin by inoculating an individual with an expression vector encoding a hepsin protein or a fragment thereof. In another embodiment of the present invention, there are provided compns. comprising immunogenic fragments of hepsin protein or an oligonucleotide having a sequence complementary to hepsin coding sequence. In another embodiment of the present invention, there is provided a method of screening for compds. that inhibit hepsin activity.

L13 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:97896 CAPLUS
DN 138:151641
TI Primers for detection of hepsin, metallo, serine and cysteine proteinases and their in diagnosis of ovarian and other cancers and therapeutic use
IN O'Brien, Timothy J.; Cannon, Martin J.; Santin, Alessandro
PA The University of Arkansas For Medical Sciences, USA
SO U.S. Pat. Appl. Publ., 74 pp., Cont.-in-part of U.S. Pat. Appl. 2002 150,908.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 15

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003027181	A1	20030206	US 2002-102283	20020320
	US 6875609	B2	20050405		
	US 6268165	B1	20010731	US 2000-510738	20000222
	US 6518028	B1	20030211	US 2001-861966	20010521
	US 2002150908	A1	20021017	US 2001-919048	20010730
	US 6787354	B2	20040907		
	US 2003077618	A1	20030424	US 2002-135795	20020430
	US 2004166117	A1	20040826	US 2003-652993	20030829
PRAI	US 2000-510738	A3	20000222		
	US 2001-861966	A2	20010521		
	US 2001-919048	A2	20010730		
	US 1997-41404P	P	19970319		
	US 1998-39211	A2	19980314		
	US 2002-102283	A2	20020320		
	US 2002-135795	A2	20020430		

AB The disclosed nucleic acid primer sets, used in combination with quant. amplification (PCR) of tissue cDNA, can indicate the presence of specific proteases in a tissue sample. Specifically, the present invention relates to expression of hepsin protease. The detected proteases are themselves specifically over-expressed in certain cancers, and the presence of their genetic precursors may serve for early detection of associated ovarian and other malignancies, and for the design of interactive therapies for cancer treatment.

RE.CNT 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:794198 CAPLUS
DN 137:308852
TI Hepsin mRNA synthesis correlated with increased susceptibility for cancer and its use in diagnosis
IN O'Brien, Timothy J.; Cannon, Martin J.; Santin, Alessandro
PA The Board of Trustees of the University of Arkansas, USA
SO U.S. Pat. Appl. Publ., 66 pp., Cont.-in-part of U.S. Ser. No. 861,966.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 15

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002150908	A1	20021017	US 2001-919048	20010730
	US 6787354	B2	20040907		
	US 6268165	B1	20010731	US 2000-510738	20000222
	US 6518028	B1	20030211	US 2001-861966	20010521
	US 2003027181	A1	20030206	US 2002-102283	20020320
	US 6875609	B2	20050405		
	US 2003077618	A1	20030424	US 2002-135795	20020430
	US 2004166117	A1	20040826	US 2003-652993	20030829
PRAI	US 1997-41404P	P	19970319		
	US 2000-510738	A3	20000222		
	US 2001-861966	A2	20010521		
	US 1998-39211	A2	19980314		
	US 2001-919048	A2	20010730		
	US 2002-102283	A2	20020320		
	US 2002-135795	A2	20020430		

AB The disclosed nucleic acid primer sets, used in combination with quant. amplification (PCR) of tissue cDNA, can indicate the presence of specific proteases in a tissue sample. Specifically, the present invention relates to expression of hepsin. The detected proteases are themselves specifically overexpressed in certain cancers, and the presence of their genetic precursors may serve for early detection of associated ovarian and other malignancies, and for the design of interactive therapies for cancer treatment.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 14:51:34 ON 27 JUN 2006)

FILE 'CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIOBASE' ENTERED AT 14:52:01 ON 27 JUN 2006
L1 79 S HEPSIN AND ANTIBODY
L2 2 S (MODIFIED HEPSIN)
L3 1 S (HEPSIN VARIANT)
L4 1 S L1 AND L3
L5 1 DUPLICATE REMOVE L2 (1 DUPLICATE REMOVED)

FILE 'CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIOBASE' ENTERED AT 15:05:22 ON 27 JUN 2006
L6 83 S (HEPSIN AND (ANTIBODY OR IMMUNOGLOBULIN))
L7 25 S (HEPSIN AND (MODIFICATION OR VARIANT OR VARIATION))
L8 11 S L6 AND L7
L9 10 DUPLICATE REMOVE L8 (1 DUPLICATE REMOVED)
L10 2 S ((MODIFIED HEPSIN) AND ANTIBODY)
L11 1 DUPLICATE REMOVE L10 (1 DUPLICATE REMOVED)
L12 7 S ((HEPSIN PEPTIDE)AND (ANTIBODY OR IMMUNOGLOBULIN))

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L13             6 DUPLICATE REMOVE L12 (1 DUPLICATE REMOVED)

=> s ((hepsin protein) and (antibody or immunoglobulin))
L14            11 ((HEPSIN PROTEIN) AND (ANTIBODY OR IMMUNOGLOBULIN))

=> duplicate remove l14
DUPLICATE PREFERENCE IS 'CAPLUS, BIOTECHDS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
PROCESSING COMPLETED FOR L14
L15             8 DUPLICATE REMOVE L14 (3 DUPLICATES REMOVED)

=> d l15 bib abs 1-8

L15  ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2006 ACS on STN  DUPLICATE 1
AN   2004:701591  CAPLUS
DN   141:219982
TI   Protein and cDNA sequences of human hepsin and their uses in early
     diagnosis and immunotherapy of ovarian cancer
IN   O'Brien, Timothy J.; Cannon, Martin J.; Santin, Alessandro; Beard, John;
     Shigemasa, Kazushi
PA   USA
SO   U.S. Pat. Appl. Publ., 85 pp., Cont.-in-part of U.S. Ser. No.. 135,795.
     CODEN: USXXCO
DT   Patent
LA   English
FAN.CNT 15
     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
PI   US 2004166117         A1    20040826    US 2003-652993          20030829
     US 6268165            B1    20010731    US 2000-510738          20000222
     US 6518028            B1    20030211    US 2001-861966          20010521
     US 2002150908         A1    20021017    US 2001-919048          20010730
     US 6787354            B2    20040907
     US 2003027181         A1    20030206    US 2002-102283          20020320
     US 6875609            B2    20050405
     US 2003077618         A1    20030424    US 2002-135795          20020430
     WO 2005021582         A2    20050310    WO 2004-US28234         20040830
     WO 2005021582         A3    20060427
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
     EP 1658307            A2    20060524    EP 2004-782668          20040830
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
PRAI US 2000-510738        A3    20000222
     US 2001-861966        A2    20010521
     US 2001-919048        A2    20010730
     US 2002-102283        A2    20020320
     US 2002-135795        A2    20020430
     US 1997-41404P        P     19970319
     US 1998-39211         A2    19980314
     US 2003-652993        A     20030829
     WO 2004-US28234       W     20040830
AB   The present invention discloses the hepsin is specifically over-expressed
     in ovarian and other malignancies.  The invention provides the protein and
     cDNA sequences of human hepsin.  A number of hepsin peptides can induce
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immune responses to hepsin, thereby demonstrating the potential of these peptides in monitoring and the development of immunotherapies for ovarian and other malignancies. The invention provides methods of vaccinating an individual against hepsin or produce immune-activated cells directed toward hepsin by inoculating an individual with an expression vector encoding a **hepsin protein** or a fragment thereof. The invention also provides methods of inhibiting expression of hepsin in a cell by introducing into a cell a vector encoding an antisense hepsin RNA or an **antibody** that binds the **hepsin protein** . The genes which are clearly overexpressed include the serine proteases hepsin, stratum corneum chymotrypsin enzyme (SCCE), protease M TADG12, TADG14 and the metalloprotease PUMP-1 protease.

L15 ANSWER 2 OF 8 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2004-13624 BIOTECHDS
TI New isolated, modified hepsin molecule, or its fragment or derivative, comprising a substitute activation sequence, useful for treating cancer, e.g. prostate, testis, stomach, thyroid, pancreatic or ovarian cancer; recombinant protein production via plasmid expression in host cell for use in disease therapy
AU PARRY G; VOGEL D; WHITLOW M; WU Q
PA SCHERING AG
PI WO 2004033630 22 Apr 2004
AI WO 2003-US31219 2 Oct 2003
PRAI US 2002-416038 4 Oct 2002; US 2002-416038 4 Oct 2002
DT Patent
LA English
OS WPI: 2004-340901 [31]
AN 2004-13624 BIOTECHDS
AB DERWENT ABSTRACT:
NOVELTY - An isolated, modified hepsin molecule, or its fragment or derivative, comprising a substitute activation sequence, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following: (1) an activated modified hepsin molecule, comprising a substitute activation sequence cleaved by a protease; (2) a method for detecting hepsin cleavage activity in a sample; (3) an isolated nucleic acid molecule encoding the modified hepsin molecule; (4) a complementary nucleic acid molecule, comprising a nucleotide sequence complementary to the nucleic acid molecule; (5) a vector comprising the nucleic acid molecule; (6) a host vector system comprising the vector in a suitable host cell; (7) a method for detecting in a sample the presence of a nucleic acid molecule encoding a modified hepsin molecule; (8) a method for inducing an immune response in a subject; (9) a method for producing an **antibody**; (10) an **antibody**, or its fragment or derivative, which binds a modified hepsin molecule; (11) an Fab, F(ab')2 or Fv fragment of the **antibody**; (12) a recombinant protein comprising the antigen-binding region of the **antibody**; (13) an **antibody** which competes for binding to the same epitope as the epitope bound by the **antibody**; (14) an idiotypic **antibody** of the modified hepsin molecule; (15) an immunoconjugate comprising the **antibody** to a therapeutic agent; (16) a hybridoma, which produces the **antibody**, or deposited with the American Type Culture Collection and designated ATCC PTA-4561; (17) a monoclonal **antibody** produced by the hybridoma; (18) a pharmaceutical composition, comprising the **antibody**, or the molecule, and a suitable carrier; (19) a method for binding a hepsin molecule; (20) a method for detecting a hepsin molecule; (21) a method for detecting the presence of hepsin molecule in a subject; (22) a method for diagnosing a cancer expressing hepsin in a subject;(23) a method for measuring the prognosis of a cancer expressing hepsin molecule in a subject; (24) a method for monitoring the course of a cancer expressing hepsin molecule in a subject; (25) a method for inhibiting growth of a cell expressing hepsin molecule; (26) a method for killing a cell expressing hepsin; (27) a method for inhibiting metastasis of a cancer

cell expressing hepsin; (28) a method for inhibiting angiogenesis of a cancer cell expressing hepsin; (29) a method for producing an **antibody** that recognizes endogenous hepsin; (30) a vaccine comprising the molecule; and (31) a kit comprising the nucleic acid molecule.

BIOTECHNOLOGY - Preferred Molecule: The nucleic acid molecule comprises the substitute activation sequence that replaces a wild-type activation sequence Arg-Ile-Val-Gly-Gly (I). The substitute activation sequence is Asp-Asp-Asp-Asp-Lys-Ile-Val-Gly-Gly (II). The substitute activation sequence is recognized and cleaved by a protease, preferably serine protease. The substitute activation sequence is recognized and cleaved by a type II transmembrane protease, or enterokinase. It is recognized and cleaved by thrombin, clotting factor Xa, furin, trypsin, chymotrypsin, elastase, thrombin, plasmin, kallikrein, aerosin, human airway trypsin-like protease (HAT), mast cell tryptase, MBL-associated serine proteases (MASP-1 and MASP-2), corin, MT-SP1/matryptase, TMPRSS2 or Stubble-stubbloid. The isolated molecule further comprises a signal peptide sequence. The signal peptide sequence is bacterial, fungal, insect, plant, or animal. The signal peptide is an Ig-kappa signal sequence. The isolated molecule further comprises an epitope tag. The epitope tag is an amino acid tag. The epitope tag is histidine or cysteine. The epitope tag is V5 or flag. The isolated molecule is from a prokaryote or eukaryote source. The eukaryote is a mammal. The mammal is bovine, porcine, murine, equine, canine, feline, avian, piscine, ovine, insects, simian, or human animal. The substitute activation sequence has been cleaved thereby producing a modified activated hepsin molecule. The nucleic acid molecule is DNA or RNA. It is a peptide nucleic acid molecule (PNA), or phosphorothioate derivative molecule. The nucleic acid molecule is labeled so as to directly or indirectly produce a detectable signal with a compound selected from a radiolabel, an enzyme, a chromophore and a fluorescer. Preferred Method: Detecting hepsin cleavage activity in a sample comprises contacting the functionally-active hepsin molecule with a substrate under conditions so that the functionally active hepsin molecule cleaves the substrate and detecting the substrate cleavage products thus indicating hepsin cleavage activity. The substrate is a chromogenic or fluorogenic substrate. The substrate is N-benzoyl-Leu-Ser-Arg-pNA.HCl, N-benzoylIle-Glu-Phe-Ser-Arg-pNA.HCl, or N-benzoyl-Phe-Val-Arg-pNA.HCl. Detecting in a sample the presence of a nucleic acid molecule encoding a modified hepsin molecule, comprises contacting the sample with the nucleic acid molecule, and detecting a complex formed between the nucleic acid molecule and a constituent in the sample or between the complementary nucleic acid molecule and a constituent in the sample, where the complex indicates the presence of the nucleic acid molecule encoding a modified hepsin molecule in the sample. The constituent is an RNA or cDNA molecule. The sample is a tissue, a cell, or a biological fluid. The biological fluid is urine, blood sera or phlegm. The sample is from prostate, liver, kidney, pancreas, stomach, thyroid, testes, or ovary. Inducing an immune response in a subject, comprises administering the modified hepsin molecule to the subject. Producing an **antibody** comprises administering the modified hepsin molecule to a subject. The subject is a hepsin knock-out mouse. Binding a hepsin molecule comprises contacting a sample with the **antibody** so as to bind the hepsin molecule. Detecting a hepsin molecule comprises contacting a sample with the **antibody**, and detecting the binding of the **antibody** with the hepsin molecule in the sample. The detecting comprises determining whether a complex is frothed between the hepsin molecule and the **antibody**, where the complex indicates the presence of the hepsin molecule in the sample. Detecting the presence of hepsin molecule in a subject comprises administering to the subject the **antibody**, and detecting the binding of the hepsin molecule with the **antibody** with the hepsin molecule in the subject. The detecting comprises determining whether a complex is formed between the hepsin molecule and the **antibody**, where the complex indicates the presence of the hepsin

molecule in the subject. Diagnosing a cancer expressing hepsin in a subject comprises quantitatively determining in a sample from the subject the amount of a hepsin molecule using the **antibody**, and comparing the amount of the hepsin molecule in a sample from a normal subject, the presence of a measurably different amount of the hepsin molecule between the sample from the subject and the sample from the normal subject indicating the presence of a cancer expressing hepsin in the subject. Measuring the prognosis of a cancer expressing hepsin molecule in a subject, comprises quantitatively determining in a sample from the subject the amount of a hepsin molecule using the **antibody**, and comparing the amount of the hepsin molecule in a sample from a normal subject, the presence of a measurably different amount of the hepsin molecule between the sample from the subject and the sample from the normal subject indicating the prognosis of the cancer expressing hepsin in the subject. Monitoring the course of a cancer expressing hepsin molecule in a subject, comprising quantitatively determining in a fkst sample from the subject the amount of a hepsin molecule using the **antibody**, and comparing the amount so determined with the amount of hepsin molecule present in a second sample from the subject, wherein the first and second samples are obtained from the subject at different points in time, a difference in the amounts of hepsin molecule in the first and second sample being indicative of the course of the cancer expressing hepsin molecule in the subject. Inhibiting growth of a cell expressing hepsin molecule comprises contacting the cell with the **antibody**, so as to inhibit growth of the cell. Killing a cell expressing hepsin comprises contacting the cell with the **antibody** so as to kill the cell. Inhibiting metastasis of a cancer cell expressing hepsin comprises contacting the cancer cell with the **antibody**. Inhibiting angiogenesis of a cancer cell expressing hepsin, comprises contacting the cell with the **antibody**. The cell is from a prostate, prostate cancer, metastasis of prostate cancer, liver, liver cancer, metastasis of liver cancer, kidney, kidney cancer, metastasis of kidney cancer, pancreas, pancreatic cancer, metastasis of pancreatic cancer, stomach, stomach cancer, metastasis of stomach cancer, thyroid, thyroid cancer, metastasis of thyroid cancer, testes, testicular cancer, metastasis of testicular cancer, ovary, ovarian cancer, or metastasis of ovarian cancer. Producing an **antibody** that recognizes endogenous hepsin, comprises administering a modified hepsin molecule to a subject and producing the **antibody**. Preferred Vector: The vector is a plasmid, cosmid, BAC, YAC, PAC or a phagemid. The host vector system comprises suitable host cell that is a prokaryotic or eukaryotic cell. The prokaryotic cell is a bacterial cell. The eukaryotic cell is a yeast, plant, insect or mammalian cell. The he insect cell is Sf21. Preferred **Antibody**: The **antibody** is a polyclonal **antibody** or monoclonal **antibody**. It can also be a chimeric **antibody** comprising a human region and a murine region. The **antibody** is humanized or neutralizing. Preferred Immunoconjugate: The immunoconjugate comprises a therapeutic agent that is a cytotoxic agent. The cytotoxic agent is selected from ricin, doxorubicin, daunorubicin, taxol, ethiduim bromide, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicine, dihydroxy anthracin dione, actinomycin D, diphteria toxin, Pseudomonas exotoxin (PE) A, PE40, abrin, glucocorticoid and radioisotopes. Preferred Composition: The pharmaceutical composition comprises a suitable carrier selected from phosphate buffered saline solution, water, emulsions, oil/water emulsion, wetting agents, sterile solutions, excipients, starch, milk, sugar, clay, gelatin, stearic acid, salts of stearic acid, magnesium stearate, calcium stearate, talc, vegetable fats or oils, gums, and glycols. It is formulated as a liposome, polymeric composition, or polymer microsphere. It is formulated as a tablet, coated tablet, or capsule.

ACTIVITY - Cytostatic. No biological data given.

MECHANISM OF ACTION - None given.

USE - The molecule is useful for treating cancer, e.g. prostate,

testis, stomach, thyroid, pancreatic or ovarian cancer.
EXAMPLE - No relevant example given. (160 pages)

L15 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
AN 2003:319344 CAPLUS
DN 138:349663
TI Hepsin protease as a tumor marker, and methods for the early diagnosis and therapy of ovarian cancer and other malignancies
IN O'Brien, Timothy J.; Cannon, Martin J.; Santin, Alessandro
PA USA
SO U.S. Pat. Appl. Publ., 43 pp., Cont.-in-part of U.S. Ser. No. 102,283.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 15

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2003077618	A1	20030424	US 2002-135795	20020430
	US 6268165	B1	20010731	US 2000-510738	20000222
	US 6518028	B1	20030211	US 2001-861966	20010521
	US 2002150908	A1	20021017	US 2001-919048	20010730
	US 6787354	B2	20040907		
	US 2003027181	A1	20030206	US 2002-102283	20020320
	US 6875609	B2	20050405		
	US 2004166117	A1	20040826	US 2003-652993	20030829
PRAI	US 2000-510738	A3	20000222		
	US 2001-861966	A2	20010521		
	US 2001-919048	A2	20010730		
	US 2002-102283	A2	20020320		
	US 1997-41404P	P	19970319		
	US 1998-39211	A2	19980314		
	US 2002-135795	A2	20020430		

AB The disclosed nucleic acid primer sets, used in combination with quant. amplification (PCR) of tissue cDNA, can indicate the presence of specific proteases in a tissue sample. Specifically, the present invention relates to expression of hepsin protease. The detected proteases are themselves specifically over-expressed in certain cancers, and the presence of their genetic precursors may serve for early detection of associated ovarian and other malignancies, and for the design of interactive therapies for cancer treatment. There are provided methods of vaccinating an individual against hepsin or produce immune-activated cells directed toward hepsin by inoculating an individual with an expression vector encoding a **hepsin protein** or a fragment thereof. In another embodiment of the present invention, there are provided compns. comprising immunogenic fragments of **hepsin protein** or an oligonucleotide having a sequence complementary to hepsin coding sequence. In another embodiment of the present invention, there is provided a method of screening for compds. that inhibit hepsin activity.

L15 ANSWER 4 OF 8 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2003-20367 BIOTECHDS
TI Detecting malignant hyperplasia in a biological sample e.g. blood, urine, saliva, tears, by isolating mRNA from the sample, and detecting hepsin mRNA in the sample for the presence or absence of the mRNA in the sample; recombinant vector-mediated gene transfer and expression in host cell for use in diagnosis and therapy
AU O'BRIEN T J; CANNON M J; SANTIN A
PA O'BRIEN T J; CANNON M J; SANTIN A
PI US 2003027181 6 Feb 2003
AI US 2002-102283 20 Mar 2002
PRAI US 2002-102283 20 Mar 2002; US 2000-510738 22 Feb 2000
DT Patent
LA English
OS WPI: 2003-531460 [50]

AN 2003-20367 BIOTECHDS

AB DERWENT ABSTRACT:

NOVELTY - Detecting (M1) malignant hyperplasia in a biological sample, comprising isolating mRNA from the sample, and detecting hepsin mRNA in the sample, where the presence or absence of hepsin mRNA in the sample is indicative of the presence or absence of malignant hyperplasia, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) inhibiting (M2) expression of endogenous hepsin in a cell, by introducing into the cell, a vector comprising a hepsin gene operably linked in opposite orientation to elements necessary for expression, where expression of the vector in the cell produces hepsin antisense mRNA that hybridizes to endogenous hepsin mRNA, therefore inhibiting expression of endogenous hepsin or its fragment, in the cell; (2) inhibiting (M3) **hepsin protein** in a cell, by introducing into the cell, an **antibody** which is specific for a **hepsin protein** or its fragment, where binding of the **antibody** to the **hepsin protein** inhibits **hepsin protein** in the cell; (3) targeted therapy (M4) to an individual, by administering a compound to an individual, where the compound has a therapeutic group and a targeting group specific for hepsin; (4) vaccinating (M5) an individual against hepsin, by inoculating an individual with **hepsin protein** or its fragment, where the inoculation with the **hepsin protein** elicits an immune response in the individual, therefore vaccinating the individual against hepsin; (5) producing (M6) immune-activated cells directed towards hepsin, by exposing immune cells to a **hepsin protein**, where the exposure to the **hepsin protein** activates the immune cells, therefore producing immune-activated cell directed towards hepsin; (6) an immunogenic composition comprising a fragment of a **hepsin protein** and an appropriate adjuvant; (7) an oligonucleotide (I) having a sequence complementary to a sequence (S1), or its fragment; (8) a composition comprising (I) and a carrier; (9) screening for compounds that inhibit hepsin activity, by contacting a sample comprising **hepsin protein** with a compound, and assaying for hepsin protease activity, where a decrease in the hepsin protease activity in the presence of the compound relative to hepsin protease activity in the absence of the compound indicates the compound inhibits hepsin activity.

Trp-Pro-Trp-Gln-Val-Ser-Leu-Arg-Tyr (S1)

BIOTECHNOLOGY - Preferred Method: (M1) further involves comparing the hepsin mRNA to reference information, where the comparison provides a diagnosis or determines a treatment of the malignant hyperplasia. The detection of the hepsin mRNA is done by PCR which uses primers selected from TGTCCCGATGGCGAGTGTTT and CCTGTTGGCCATAGTACTGC. In (M3), the **hepsin protein** group is selected from 19 sequences e.g. (S2-6). In (M4), the targeting group is selected from an **antibody** specific for hepsin and a ligand binding domain that binds hepsin. The therapeutic group is selected from radioisotope, toxin, chemotherapeutic agent, an immune stimulant and a cytotoxic agent. In (M5), the length of the hepsin fragment is 9-20 residue long. The 9 residue fragment is selected from e.g. (S2-6). In (M6), the immune cells are selected from B or T cells, or dendritic cells which are isolated from an individual prior to the exposure, where the activated dendritic cells are reintroduced into the individual subsequent to the exposure.

Tyr-Tyr-Gly-Gln-Gln-Ala-Gly-Val-Leu (S2) Ser-Leu-Gly-Arg-Trp-Pro-Trp-Gln-Val (S3) Ser-Leu-Leu-Ser-Gly-Asp-Trp-Val-Leu (S4) Gly-Leu-Gln-Leu-Gly-Val-Gln-Ala-Val (S5) Lys-Val-Ser-Asp-Phe-Arg-Glu-Trp-Ile (S6)

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Inhibitor of expression of endogenous hepsin in a cell; Elicitor of immune response. No biological data given.

USE - (M1) is useful for detecting malignant hyperplasia in a biological sample such as blood, urine, saliva, tears, interstitial fluid, ascites fluid, tumor tissue biopsy and circulating tumor cells.

(M2) is useful for inhibiting expression of endogenous hepsin in a cell, and (M3) is useful for inhibiting **hepsin protein** in a cell. (M4) is useful for a targeted therapy to an individual, where the individual suffers from cancer selected from ovary, lung, prostate, and colon. (M5) is useful for vaccinating an individual against hepsin, where the individual has cancer, is suspected of having cancer or is at risk of getting cancer. (I) is useful for treating a neoplastic state e.g. cancer in an individual (all claimed).

EXAMPLE - No suitable example given.(74 pages)

L15 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
AN 2002:637879 CAPLUS
DN 137:180862
TI Protein and cDNA sequences of an amplified human cancer gene hepsin, its diagnostic and therapeutical uses thereof
IN Mu, David; Powers, Scott
PA Tularik Inc., USA
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2002064839	A2	20020822	WO 2002-US4018	20020212
WO 2002064839	A3	20030227		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2438433	AA	20020822	CA 2002-2438433	20020212
US 2003049645	A1	20030313	US 2002-73060	20020212
EP 1373565	A2	20040102	EP 2002-706233	20020212

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRAI US 2001-268361P	P	20010214	
WO 2002-US4018	W	20020212	

AB The present invention provides nucleic acid and protein sequences for a novel human gene, hepsin, and methods, reagents, and kits for diagnosing and treating cancer in a mammal, e.g., a human. This invention is based upon the discovery that the novel hepsin is overexpressed and/or amplified in cancer tissues, such as prostate cancer, breast cancer, lung cancer and ovary cancer. Gene hepsin, is originally identified as a gene encoding trypsin-like serine protease. Methods to detect cancer or a propensity to develop cancer, to monitor the efficacy of a cancer treatment, and to treat cancer, by inhibiting the expression and/or activity of hepsin in a cancer cell are included.

L15 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:755101 CAPLUS
DN 137:289992
TI Protein, gene and cDNA sequences of a novel human protease related to hepsin and their uses in drug screening
IN Gan, Weiniu; Ye, Jane; Di Francesco, Valentina; Beasley, Ellen M.
PA USA
SO U.S. Pat. Appl. Publ., 55 pp.
CODEN: USXXCO
DT Patent

LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2002142440	A1	20021003	US 2001-820002	20010329
	US 6482630	B2	20021119		
	CA 2442829	AA	20021010	CA 2002-2442829	20020328
	WO 2002079228	A2	20021010	WO 2002-US9430	20020328
	WO 2002079228	A3	20030213		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	AU 2002258630	A1	20021015	AU 2002-258630	20020328
	EP 1383907	A2	20040128	EP 2002-728586	20020328
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	US 2003129726	A1	20030710	US 2002-274031	20021021
	US 7037705	B2	20060502		
	US 2005250154	A1	20051110	US 2005-182752	20050718
PRAI	US 2001-820002	A	20010329		
	WO 2002-US9430	W	20020328		
	US 2002-274031	A3	20021021		

AB The invention provides protein, cDNA and genomic sequences for a novel human protease related to hepsin. Specifically, a virtual northern blot shows hepsin gene expression in the liver, prostate, T cells from T cell leukemia, hepatocellular carcinoma, and lung tumor. Twelve single nucleotide polymorphism, including 3 indels, has been found on hepsin gene mapped to chromosome 19. The invention also relates to screening modulator of hepsin and use them in therapy. The invention further relates to methods, vector and hosts for expression of hepsin.

L15 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:560004 CAPLUS
DN 135:148191
TI Methods for the early diagnosis of ovarian cancer
IN O'brien, Timothy L.
PA Board of Trustees of the University of Arkansas, USA
SO U.S., 68 pp., Cont.-in-part of U.S. Ser. No. 39,211.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 15

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6268165	B1	20010731	US 2000-510738	20000222
	US 6303318	B1	20011016	US 1998-39211	19980314
	CA 2400703	AA	20010830	CA 2001-2400703	20010220
	WO 2001062271	A1	20010830	WO 2001-US5703	20010220
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 1257287	A1	20021120	EP 2001-914444	20010220
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

	JP 2003523524	T2	20030805	JP 2001-561336	20010220
	US 6518028	B1	20030211	US 2001-861966	20010521
	US 2002150908	A1	20021017	US 2001-919048	20010730
	US 6787354	B2	20040907		
	US 2003027181	A1	20030206	US 2002-102283	20020320
	US 6875609	B2	20050405		
	US 2003077618	A1	20030424	US 2002-135795	20020430
	US 2004166117	A1	20040826	US 2003-652993	20030829
PRAI	US 1997-41404P	P	19970319		
	US 1998-39211	A2	19980314		
	US 2000-510738	A	20000222		
	WO 2001-US5703	W	20010220		
	US 2001-861966	A2	20010521		
	US 2001-919048	A2	20010730		
	US 2002-102283	A2	20020320		
	US 2002-135795	A2	20020430		

AB The disclosed nucleic acid primer sets, used in combination with quant. amplification (PCR) of tissue cDNA, can indicate the presence of specific proteases in a tissue sample. The detected proteases are themselves specifically overexpressed in certain cancers, and the presence of their genetic precursors may serve for early detection of associated ovarian and other malignancies, and for the design of interactive therapies for cancer treatment. In one embodiment of the present invention, there is provided a method of diagnosing cancer in an individual, comprising the steps of obtaining a biol. sample from an individual and detecting hepsin in the sample. The presence of hepsin in the sample is indicative of the presence of carcinoma in the individual.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 8 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
AN 2002-00919 BIOTECHDS
TI New oligonucleotide complementary to hepsin encoding sequence, useful for treating cancer and screening for compounds that inhibit hepsin;
vector expression in host cell for recombinant protein gene production useful in gene therapy
AU O'Brien T J
PA Univ.Arkansas
LO Little Rock, AR, USA.
PI WO 2001062271 30 Aug 2001
AI WO 2001-US5703 20 Feb 2001
PRAI US 2000-510738 22 Feb 2000
DT Patent
LA English
OS WPI: 2001-582004 [65]
AN 2002-00919 BIOTECHDS
AB An oligonucleotide (I) having a complementary sequence to a fully defined sequence (S1) of 1,783 bp is claimed. Also claimed are: treating a neoplastic state in an individual in need of such treatment; screening for compounds that inhibit hepsin activity; diagnosing (M1) cancer in an individual by detecting hepsin in a biological sample, where the detection is carried out by DNA array or DNA chip; detecting (M2 or M3) malignant hyperplasia in a biological sample; inhibiting expression of endogenous hepsin in a cell by introducing a vector into a cell; targeted therapy (M4) to an individual by administering a compound; vaccinating (M5) an individual against hepsin; and producing (M6) immune-activated cells directed towards hepsin. The oligonucleotide is useful for detection of cancer, treatment of cancer and screening for compounds that inhibit hepsin activity. Hepsin protease, mRNA and immunospecific anti-hepsin **antibodies** are useful for diagnosis of cancer in an individual. (77pp)

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=> d his

     (FILE 'HOME' ENTERED AT 14:51:34 ON 27 JUN 2006)

     FILE 'CAPLUS, BIOENG, BIOTECHNO, BIOTECHDS, ESBIOBASE' ENTERED AT
     14:52:01 ON 27 JUN 2006
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L2             2 S (MODIFIED HEPSIN)
L3             1 S (HEPSIN VARIANT)
L4             1 S L1 AND L3
L5             1 DUPLICATE REMOVE L2 (1 DUPLICATE REMOVED)

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     15:05:22 ON 27 JUN 2006
L6            83 S (HEPSIN AND (ANTIBODY OR IMMUNOGLOBULIN))
L7            25 S (HEPSIN AND (MODIFICATION OR VARIANT OR VARIATION))
L8            11 S L6 AND L7
L9            10 DUPLICATE REMOVE L8 (1 DUPLICATE REMOVED)
L10            2 S ((MODIFIED HEPSIN) AND ANTIBODY)
L11            1 DUPLICATE REMOVE L10 (1 DUPLICATE REMOVED)
L12            7 S ((HEPSIN PEPTIDE)AND (ANTIBODY OR IMMUNOGLOBULIN))
L13            6 DUPLICATE REMOVE L12 (1 DUPLICATE REMOVED)
L14           11 S ((HEPSIN PROTEIN) AND (ANTIBODY OR IMMUNOGLOBULIN))
L15            8 DUPLICATE REMOVE L14 (3 DUPLICATES REMOVED)
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